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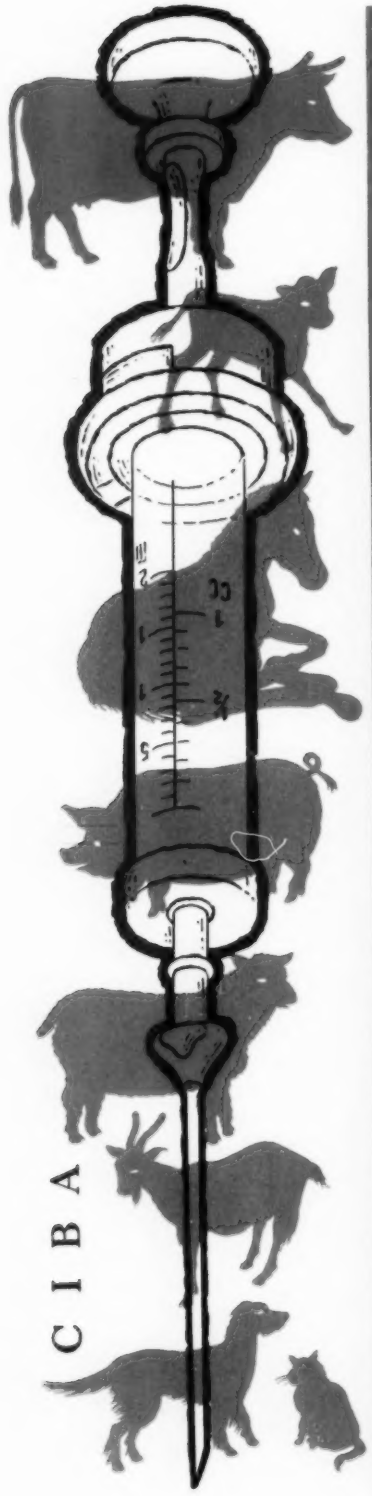

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Muscle Relaxants in Veterinary Anaesthesia*

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MANY surgical interferences and diagnostic procedures are more easily carried out if muscle tone is reduced or abolished and often one of the main purposes of anaesthesia is to achieve this relaxation of the skeletal muscles. It is believed that muscle tone is caused by a slow asynchronous discharge of impulses from cells in the ventral horn region of the spinal cord. The ventral horn cells are controlled by impulses in the afferent fibres from the muscle spindles.

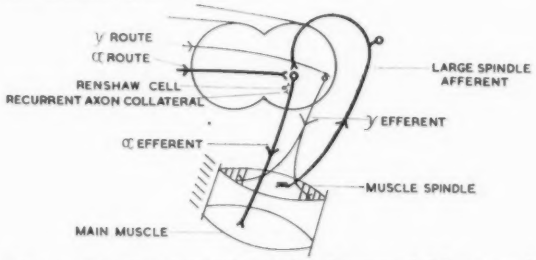

FIG. 1.—The muscle spindle. (After Hammond, Merton and Sutton, *Brit. Med. Bull.*, 1956, vol. 12, p. 214.)

The muscle spindle lies in parallel with the main muscle (Fig. 1) and its fast conducting afferent is in synaptic connexion with the large α-motor neurone supplying the main muscle fibres. A slow conducting γ-motor fibre supplies the contractile poles of the spindle and can thus alter the bias on the spindle sensory endings. The muscle can be made to contract either by impulses from higher centres exciting the α-motor neurone (the α-route) or by impulses in the γ-efferents (the γ-route) which activate the muscle indirectly *via* the stretch-reflex arc (Hammond, Merton & Sutton, 1956).

During anaesthesia abolition of muscle tone and ability to contract can be brought about in 3 ways.

The first of these ways is by the use of narcotic drugs such as ether, chloroform, halothane, chloral hydrate and the barbiturates. These narcotic drugs produce a graded depression of the central nervous system and muscle relaxation probably results from this depression being reflected in the activity of ventral horn cells. There is no doubt that a profound degree of muscle relaxation can be obtained when a potent narcotic drug is administered in doses which produce a deep generalised depression of the central nervous system. However, the consequences of such a generalised depression are widespread. For example, the activity of the respiratory centre is impaired if not abolished. This, in itself, is perhaps of little significance during an operation, for respiration can be maintained by artificial means, but any residual respiratory depression, or depression of the cough reflex, post-operatively, due to slow elimination of the anaesthetic agent may produce dire results. Even more serious is the coincidental impairment of the central nervous mechanism responsible for the control of the cardiovascular system. Depression of the medullary vasomotor centres contributes to the advent of circulatory failure during operation and may result in severe hypotension following quite small degrees of haemorrhage. Furthermore, the deeply narcotised animal loses the ability to compensate for movement and changes of posture. Finally, after deep anaesthesia there is likely to be a period of narcosis, depression and immobility which can predispose to the onset of respiratory complications such as pneumonia in horses and aspiration of regurgitated ingesta in ruminants. In short, muscle relaxation can be obtained by the use of drugs which act upon the central nervous system but it is obtained at a high price—and the price is paid by the patient.

The second and third methods of producing muscle relaxation utilise drugs which have a peripheral, rather than central, action. Injecting local analgesic drugs directly into the muscle mass, or around nerve fibres or nerve endings, isolates the muscle fibre from

* A Peter Wilson Bequest Lecture delivered at the Royal (Dick) School of Veterinary Studies, Edinburgh, on March 9th, 1960.

nervous influences, for these drugs block conduction in the nerves. This method, too, has its disadvantages. Clearly the temperament of the animal is important, and the temperament of some animals is such as to render them unsuitable subjects for the use of local analgesic techniques. The time factor is also important. Many of the procedures are time consuming in that many injections have to be made. Furthermore, even after the simplest of techniques there is a delay before the full degree of analgesia is attained. In addition to these disadvantages, such techniques as epidural and spinal blocks produce a loss of control of much of the circulatory system as a result of paralysis of the sympathetic nerves.

The third way of abolishing muscle tone is by blocking transmission at the myoneural junction itself. This, again, is a peripheral effect which can be produced by certain drugs—drugs known as "muscle relaxants," or more simply as "relaxants." A relaxant may be defined as a drug other than a general anaesthetic or local analgesic agent which is used in anaesthesia and therapeutics to produce either relaxation or paralysis in voluntary striated muscle. In general, they do not cause any depression of the central nervous or circulatory systems and by their use it is possible for an anaesthetist to produce instantly, and with certainty, any degree of muscular relaxation without influencing the excitability and functioning of the central nervous and cardiovascular systems as a whole.

It is no exaggeration to say that the use of relaxant drugs has, in man, completely revolutionised anaesthetic practice. In veterinary anaesthesia relaxants have been in use for a period of about 10 years, and it is now possible to make some appraisal of their value in this field. First, however, it is essential to understand the phenomena which occur at the myoneural junction upon the arrival of a motor nerve impulse, and the ways in which neuromuscular block can be produced. Once these phenomena are appreciated an accurate evaluation can be made for it becomes possible to distinguish which of the signs observed after the administration of relaxant drugs are due to the drug administered, and which are due to other factors such as anaesthetic mismanagement.

All the observed facts relating to neuromuscular transmission and block do not quite fit into any one pattern, and the theories of neuromuscular block must still be accepted with some reserve. The following description does, however, attempt to outline the picture in so far as it is known at the present time.

Normal Neuromuscular Transmission

However long a motor nerve fibre may be, it eventually terminates in juxtaposition to a muscle fibre. Since, as has already been noted, relaxant drugs act at the neuromuscular junction the way in which activity is induced at this junction is of particular interest to anaesthetists.

The detailed anatomy of the neuromuscular junction has been studied by Robertson (1956) in the chameleon lizard. As the nerve fibre approaches the myoneural junction the endoneural sheath is shed, so that it is then covered only by a double membrane complex referred to as the Schwann or axoplasmatic membrane. Essentially, this consists of 3 layers—an outer dense layer, a middle clear zone which is slightly thicker, and an inner dense layer acting as a boundary margin for the contained axoplasm. The skeletal muscle fibre is covered by 3 almost identical layers and at the neuromuscular junction the outer layer of the nerve fibre fuses with the outer layer of the muscle fibre. This combined layer together with all the other layers then proceeds to surround the nerve terminal in a series of finger-like folds which bite into the substance of the muscle fibre as a series of what are known as "junctional folds." The crucial junction between nerve and muscle, therefore, lies in this dense zone which is composed of the fusion of the two layers.

Section of the nerve terminal and examination under the electron microscope reveals a considerable number of mitochondria and numerous small vesicular bodies scattered through the axoplasm (Robertson, 1956).

It is now generally agreed that an impulse is transmitted from nerve fibre to muscle fibre by chemical means and what has become known as the "chemical theory of neuromuscular transmission" is an accepted part of neurophysiology. This theory has grown out of the observation of Dale and his co-workers (Dale, Feldberg & Vogt, 1936) in 1936 that stimulation of the motor nerve to a perfused muscle produces a substance in the perfusate which has all the pharmacological characteristics of acetylcholine, and that the close arterial injection of acetylcholine produces a brief tetanic contraction in dog or cat muscle (Brown, Dale & Feldberg, 1936). Basically, the chemical theory of neuromuscular transmission postulates that when an impulse travels down a motor nerve acetylcholine molecules are liberated at the nerve-endings and react with a receptor substance (probably a protein) which resides on the surface of the muscle fibre in the specialised end-plate region. Acetylcholine causes a change in the permeability of the end-plate to all ions and thus gives rise to a variation in the resting potential of the end-plate region, and causes what is known as the "end-plate potential." The mechanism of the production of the end-plate potential involves the membrane becoming freely permeable to both anions and cations and not, as in the case of nerve or muscle, by developing a specific permeability to sodium ions alone. If the end-plate potential reaches a critical level it fires off the "spike" which is propagated as the "muscle action potential" along the sarcolemma. This is accomplished by adjacent regions of the sarcolemma discharging into the depolarised area.

The mechanism by which acetylcholine is released at the nerve terminal is not completely understood. The acetylcholine molecule is believed to be synthesised within the nerve and then held in readiness. The tubular or vesicular bodies may be intracellular corpuscles to which the acetylcholine molecules are attached. Thus one corpuscle may hold many thousands of acetylcholine molecules. These corpuscles occasionally come into contact with the surface membrane of the nerve cell and then rupture to release their cargo of acetylcholine. This explains the

sporadic release of acetylcholine which has been recognised even when the neuromuscular junction is at rest. Nevertheless, the fact that the corpuscles do not always rupture when they come into contact with the surface membrane of the nerve has given rise to the suggestion that both the corpuscles and the surface membrane possess "critical spots" and it is not until these specific areas actually meet that the rupture occurs (del Castillo & Katz, 1956). The effect of the arrival of a nerve impulse might be merely to increase the critical area on the surface membrane so that almost every corpuscle coming into contact is broken up and large quantities of acetylcholine released.

Once released, the acetylcholine molecules have to travel only 1 μ—a minute distance—before reaching their target. This very short range enables the acetylcholine molecules to excite the end-plate before being hydrolysed by "cholinesterase," a specific enzyme which destroys the acetylcholine almost as rapidly as it is produced.

The subsequent fate of the acetylcholine is rather obscure. The majority is certainly hydrolysed by cholinesterase to acetic acid and choline but some of the acetylcholine must diffuse out into the extracellular fluid.

Forms of Neuromuscular Block

Turning now to a consideration of the ways in which the impulse can be prevented from passing across the myoneural junction it soon becomes apparent that there are 2 main ways in which transmission at the neuromuscular junction may be blocked.

First, it may simply be a prolongation of the normal depolarisation process that arises at the motor end-plate in the presence of acetylcholine. Normally the effect of acetylcholine persists for only a fraction of a second, but after depolarisation has taken place there will, theoretically, be a time interval during which the muscle fibre will no longer respond to a stimulus arriving *via* the nerve fibre. In other words, for this short interval of time a state of "depolarisation block" is present. Decamethonium (C10) and suxamethonium ("Scoline") are examples of drugs that act in this manner.

Secondly, d-tubocurarine and allied drugs can prevent the passage of an impulse from nerve to muscle. They are believed to act by reason of an affinity for the protein molecules of the end-plate region but they do not excite the muscle fibre before bringing on a state of temporary neuromuscular block. The molecules of the drug are in a loose conjunction with the protein molecules of the end-plate region and although acetyl-choline liberation and destruction continues it no longer excites the muscle.

This type of block is sometimes referred to as "competitive inhibition"—"competitive" because curare competes with acetylcholine for the receptor sites at the end-plates, and "inhibition" because it inhibits the action of acetylcholine. There are, however, many other drugs which compete with acetylcholine for the motor end-plate receptors yet cannot be classified in the same group as curare. Thus to-day, the term "non-depolarisation block" is favoured as being both more descriptive and more accurate.

If a depolarising relaxant and a non-depolarising agent are given to an animal "mixed block" occurs. Some muscle fibres will be under the influence of one type of drug while others will be affected by the other agent. The practice of mixing depolarising and non-depolarising drugs is probably very unwise on pharmacological grounds and fortunately is very rarely necessary in veterinary clinical practice.

"Dual block" refers to a peculiar effect seen after the administration of depolarising drugs. The muscle fibres respond first by depolarisation but then gradually the type of response changes until it bears all the characteristics of a block due to non-depolarisation. The exact time relation and cause are, as yet, unknown. In veterinary anaesthesia this type of block is of great importance for it appears to occur more readily in some kinds of animal than in others.

Other, comparatively unimportant, variants of neuromuscular block are known. Drugs such as procaine (Harvey, 1939), and excess of magnesium ions (Paton, 1956), or a deficiency of calcium ions (Harvey & MacIntosh, 1940), all slow down, or arrest, the production of acetylcholine molecules at the nerve terminal.

It is now quite clear that the results obtained in any one species of animal with any one relaxant drug do not necessarily indicate how any other species of animal will react to that particular drug. Thus if these drugs are to be used in veterinary anaesthesia in a rational manner the way in which the various domestic animals react to the various drugs must be known and although much information is already available the picture is, as yet, by no means complete.

The Pattern of Neuromuscular Block

The one principal feature of neuromuscular block which appears to be common to all species of animal and all kinds of drug is the pattern of events as each muscle group becomes involved (Fig. 2).

This pattern holds true, with only minor variations, in all kinds of animal for both depolarising and non-depolarising relaxants. The muscles of expression, the jaw muscles and, tail muscles become paralysed within 30 to 60 seconds of the intravenous injection of the drug. Next to be affected are the limb and neck muscles. Paresis of the swallowing and phonatory muscles follows and then the abdominal muscles relax. Soon after this the intercostal muscles fail and finally the diaphragm is affected.

In the past, attempts were made to give a dose of relaxant which was just sufficient to paralyse the abdominal muscles without the intercostal muscles and diaphragm being affected. However, paralysis of the abdominal muscles is invariably associated with a marked diminution in the tidal volume of respiration and it is now generally agreed that if the abdominal muscles are paralysed with a relaxant some form of artificial respiration must be applied. This being so there is little point in trying to judge the dose of relaxant to a nicety in any particular case for any spontaneous respiratory movements which may persist after the administration of the

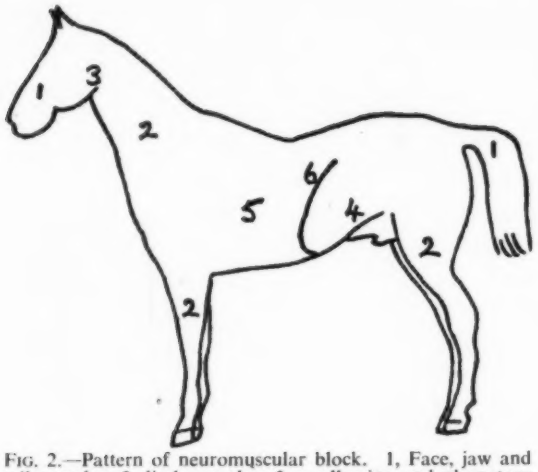

FIG. 2.—Pattern of neuromuscular block. 1, Face, jaw and tail muscles; 2, limb muscles; 3, swallowing and phonatory muscles; 4, abdominal muscles; 5, intercostal muscles; 6, diaphragm.

relaxant will soon be abolished if artificial ventilation is efficiently carried out.

Nevertheless, it is a relatively simple matter to produce a stage of paresis of the limbs with a dose of relaxant which produces no significant reduction in tidal volume and thus this technique, combined with light anaesthesia is suitable for many operations on the extremities.

Recovery from the action of the muscle relaxants depends upon a number of factors, the most important of which is the blood supply of the muscle in question. However, in general it is true to say that the sequence of events on recovery is almost a mirror image of that on paralysis. The only muscles which appear to be an exception to this rule are those involved in pathological processes. The reasons for this consistency of response and recovery are not easily determined.

Muscle Relaxants in Domestic Animals

Since both non-depolarising and depolarising agents are used in veterinary anaesthesia, their pharmacology must be studied in some detail in the various kinds of animal in which they are used.

The Non-depolarising Relaxants

The action of these drugs is comparatively easy to understand and only two, curare and gallamine, need be considered in any detail although numerous others are available.

Curare

During the middle of the nineteenth century Claude Bernard elucidated the nature of the paralysis but, largely because of the impurities of the preparations which were available, curare remained the plaything of the physiologists. Only in 1942 was a purified and biologically standardised preparation known as "Intocostrin" used in anaesthesia by Griffith and Johnson in Montreal. Even this was a comparatively crude preparation and it is surprising that more note was not taken of the work of King in London, for in 1935 King had prepared a pure crystalline alkaloid from crude curare. This quaternary alkaloid is called "d-tubocurarine" and it was d-tubocurarine chloride which was first used in this country by Gray and Halton in 1944 (Gray & Halton, 1946) and which is now the preparation of curare most extensively used in clinical practice.

Curare is believed to have the same affinity for the protein molecules of the motor end-plate as acetylcholine but it is incapable of bringing about depolarisation.

Records made at the end-plate region of frog muscle during progressive curarisation show the end-plate potential diminishing and the spike latent period increasing until finally there is a pure end-plate potential with no spike (Kuffler, 1942). Thus, when curarisation is complete there is no propagation of the muscle action potential. Conversely, as the concentration of curare in the blood-stream and tissues falls so the number of curare molecules in the end-plate diminishes until once more a point is reached where the number present is insufficient to prevent acetylcholine from reaching the end-plate and thus the spike reappears with resultant muscle contraction and resumption of muscle tone. The recovery process can be accelerated either by the direct injection of acetylcholine (which is rather impracticable) or by preventing the destruction of acetylcholine by cholinesterase, *i.e.* by administering an anti-cholinesterase such as neostigmine, which will allow the concentration of acetylcholine molecules in the end-plate region to build up. Provided the concentration of curare is not excessive this accumulation of acetylcholine leads to a reversal of the neuromuscular block and thus neostigmine is used in clinical practice as an antidote to curare and curare-like drugs.

D-tubocurarine chloride is used extensively in man and has proved to be a very reliable relaxant drug. In veterinary anaesthesia it has been used most widely in dogs. Pickett (1951) used the drug in 250 surgical cases after first carrying out experiments to determine the optimum dose. He adopted a dose of about 0.06 mg. per lb. bodyweight and reported very favourably on the use of the drug in canine anaesthesia. However, it is likely that in fact this dose produced very little beneficial effect in the type of case in which it was used. The effective dose for the dog is of the order of 0.2 mg. per lb., that is about 3 times the dose used by Pickett. Using this effective dose it soon became apparent, clinically, that the post-operative condition of dogs which had received d-tubocurarine during anaesthesia was less satisfactory than if this agent had not been used. It soon became clear that, in dogs, d-tubocurarine chloride had actions other than at the myoneural junction. It was already known that the injection of curare caused the liberation of histamine and it was shown that in dogs it also blocked transmission at the ganglionic synapses. These two effects together produce a severe fall in blood pressure (Fig. 3).

The dimethyl ether of d-tubocurarine ("d.m.e. curare") is a less potent liberator of histamine, and with this compound the fall in blood pressure is

not quite so severe. Nevertheless, clinically there appears to be little to choose between these two preparations of d-tubocurarine.

The use of anti-histamine drugs and vasopressors is not always practicable or even desirable and, therefore, it is now clear that d-tubocurarine should not be used as a relaxant in dogs.

Booth and Rankin (1953) studied the pharmacology of d-tubocurarine in horses. Doses of 0.06 mg. per lb. bodyweight given by rapid intravenous injection caused paralysis of limb muscles without producing respiratory paralysis and did not affect the blood pressure. These workers next studied the use of curare during chloral hydrate narcosis and came to the conclusion that this combination of drugs had no value in anaesthesia in horses. However, once again it is clear that the dose of curare used was much less than what is regarded to-day as the minimal effective dose. Curare has not been used clinically in horses to any great extent and more information on its use in modern anaesthetic procedures in horses is most desirable.

Little is known about the action of curare in ruminant animals. Young lambs and calves are very susceptible to the myoneural blocking action of curare but doses of up to 0.03 mg. per lb. bodyweight have been given to these young animals without apparent harmful effect. In adult ruminants the administration of curare, even in small doses, has resulted in the death of the animals. The cause of death in these circumstances is unknown, but it is *not*, as some Scandinavian workers have suggested, due to asphyxia or to the inhalation of regurgitated ruminal contents.

D-tubocurarine chloride in doses of 0.14 mg. per lb. bodyweight causes complete paralysis in pigs when given by rapid intravenous injection. Blood pressure falls slightly but the fall is not of clinical significance. Equi-potent doses of the dimethyl ether of d-tubocurarine also cause a similar fall in the blood pressure.

A similar, but more severe, fall in blood pressure is seen in anaesthetised cats. Fig. 4 shows the effect of the intravenous injection of 1 mg. of d-tubocurarine chloride in a 6-lb. cat anaesthetised with thiopentone/nitrous oxide/oxygen.

Gallamine Triethiodide

There is no doubt that of the non-depolarising relaxants available to-day, gallamine triethiodide ("Flaxedil") is the most useful in veterinary anaesthesia. It acts in a similar manner to curare but is without the undesirable side-effects of that substance. Gallamine has no direct action on the myocardium although it has been suggested (Riker & Wescoe, 1957) that it reduces the incidence of cardiac arrhythmias under cyclopropane anaesthesia. It has a well-marked vagal-blocking activity and this action is particularly useful during halothane anaesthesia.

Gallamine is the non-depolarising relaxant of choice in dogs. As shown in Fig. 5 it has no hypotensive effect and doses of 0.5 mg. per lb. bodyweight usually cause complete paralysis within 2 minutes of their intravenous injection. Apnoea persists for 10 to 20 minutes. Apart from causing a slight tachycardia gallamine appears to have no significant action other than at the myoneural junction.

Pigs are very resistant to gallamine. In one typical case a pig weighing 212 lb. received a total of 640 mg. of gallamine over the course of an operation which lasted for about 2½ hours.

In some cats the injection of gallamine may be followed by a transient fall in blood pressure (Fig. 6). This fall has also been reported, quite recently, by Payne (1960), and he has suggested that it may be due to gallamine having some anticholinesterase activity for it is no longer apparent after the administration of atropine and the pattern of response is very similar to that produced by the intravenous injecion of acetylcholine. Whatever the explanation of the phenomenon may be, it is not of clinical significance.

Gallamine may also be used in horses in doses of 0.25 to 0.5 mg. per lb. bodyweight. These doses cause complete paralysis, but there are very few indications for the use of this drug in clinical practice.

Laudexium Methyl Sulphate

One other non-depolarising relaxant which must be mentioned is laudexium methyl sulphate or "Laudolissin." This is a synthetic compound and in dogs it has about half the potency of d-tubocurarine. The maximum degree of relaxation is reached 4 or 5 minutes after the intravenous injection of the drug and the duration of activity is about twice that of d-tubocurarine. Neostigmine antagonises laudexium block but in 2 out of 10 dogs the improvement in respiration which followed the injection of neostigmine was not maintained and it is possible that in view of the prolonged action of laudexium the activity of the neostigmine may wear off before that of the relaxant.

Laudexium has failed to gain wide popularity as a relaxant drug.

Neostigmine Methyl Sulphate

All the non-depolarising relaxants are antagonised by anticholinesterase compounds and one of these, neostigmine methyl sulphate or "Prostigmin" is used in anaesthesia. This drug prevents the destruction of acetylcholine by cholinesterase and it also has an acetylcholine-like stimulant action at the end-plate. Whenever neostigmine is to be administered it should be preceded by a dose of atropine to prevent the muscarinic effects—salivation, bradycardia, urination and defaecation—from appearing.

Fig. 7 shows the effect of neostigmine in a dog recovering from paralysis induced with gallamine. Following the injection of neostigmine the amplitude of the respiratory trace shows an almost immediate increase but initially there is a pause at the end of inspiration giving the pattern of "rectangular respiration" which, in the absence of respiratory obstruction, is usually associated with some degree of paralysis of the respiratory muscles.

The Depolarising Agents

A consideration of the other major group of relaxants, the depolarising agents, reveals a very com-

plicated picture and it must be stated at once that their mode of action is not yet completely clear.

The introduction of decamethonium (C10) and suxamethonium (succinylcholine),* both of which have many features in common with acetylcholine led some authorities to assume that both these drugs caused a neuromuscular block by persistent and total depolarisation of the motor end-plate.

This theory of total depolarisation was shown to be unacceptable by Burns and Paton (1957) who found that instead of an absence of end-plate potential there was a potential many times greater than normal. That is to say they found an end-plate potential which would be expected to fire-off the adjacent muscle membrane but for some reason it failed to do so. In fact there appeared to be an area of inexcitability of the muscle membrane around the end-plate region and Paton (1956) has likened this to a " desert area."

He stresses that this electrical inexcitability does not develop immediately, but only when depolarisation is prolonged does it occur, and its persistence is the cause of the local inexcitability. An important feature which must be emphasised is that, despite the persistence of the block the end-plate depolarisation gradually fades away until it again resumes a state of polarity.

Thesleff (1955) does not accept this work and from studies on rat muscle using intracellular recording electrodes he has come to the conclusion that during suxamethonium block there is decreased sensitivity of the end-plate to the transmitter substance (acetylcholine).

These divergent opinions are probably the result of different experimental techniques and the use of different species of experimental animals.

Further difficulties arise when this last point is considered, for while suxamethonium was believed to have a pure depolarising action in man and in cats it soon became clear (Zaimis, 1952) that in monkeys, dogs and hares this drug produces a block of an intermediate kind. That is, in the dog, hare and monkey it produces an initial depolarisation which passes off, leaving, nevertheless, a state of block which is of a non-depolarisation character. Furthermore, it now seems possible from the purely pharmacological standpoint that the depolarising drugs, may, even in man and the cat, lose some of their characteristic characters and come to behave as being, at least in part, non-depolarising relaxants. In other words, in dogs, monkeys and hares, suxamethonium produces a " dual block " and under certain circumstances, particularly if given for a long time or in large doses, it does the same thing in cats and in man. Thus, theoretically once the block has changed to one of non-depolarisation it should be antagonised by the injection of an anticholinesterase such as neostigmine and in practice this appears to be the case.

Drugs which first stimulate and then desensitise both to their own action and to that of similar substances have been known for many years and nicotine in its action on autonomic ganglia is a notable example, so that there is nothing new in this concept.

In the past great clinical emphasis has always been laid on the differences between a depolarising and a non-depolarising type of block but in reality only a thin margin separates them. In fact, in veterinary anaesthesia, the main difference may well be only the fact that the depolarising agents produce an initial muscle contraction.

Suxamethonium

Some of the pharmacological actions of suxamethonium, otherwise known as " succinylcholine " were first described in 1906 by Hunt and Taveau but its neuromuscular blocking activity was not observed because it was given to a previously curarised animal. The drug was first used in man as a neuromuscular blocking agent by Thesleff in Stockholm in 1951 and a very similar drug, suxethonium, was first used in veterinary anaesthesia by Hall in 1952 at the Royal Veterinary College, London. To-day, suxamethonium is fairly widely used in veterinary anaesthesia throughout the world.

There are wide species differences between the various domestic animals in their sensitivity to suxamethonium. The horse is resistant to the neuromuscular blocking affect of the drug. The pig and cat are also resistant, but dogs, sheep and cattle are most sensitive.

Since it is known that pseudocholinesterase can hydrolyse suxamethonium to choline and succinic acid attempts have been made to correlate the sensitivity of an animal to this drug with the level of pseudocholinesterase present in the blood of the animal. Hansson (1957) was unable to demonstrate any such correlation but it has been shown that in dogs the injection of a purified pseudocholinesterase preparation produces a marked increase in resistance to the effect of the drug (Hall *et al.*, 1953).

Since suxamethonium or " succinylcholine " is so closely related, chemically, to acetylcholine it might be expected to have other actions in the body beside its main effect of producing neuromuscular block. This is indeed the case.

Suxamethonium causes a marked rise in blood pressure, in all animals. Hansson (1958) believed that any increase in blood pressure was secondary to anoxia caused by respiratory depression. However, his experimental technique was not sound and Stevenson (1959) was able to show quite conclusively that the rise in pressure is in no way related to asphyxia. Suxamethonium obviously causes stimulation of post-ganglionic sympathetic fibres and a release of adrenal medullary hormones.

In one horse, anaesthetised with thiopentone-cyclopropane-oxygen a dose of 0.17 mg. per kg. cause the blood pressure to rise from 110/80 to 160/85 (Stevenson & Hall, 1959). In unanaesthetised horses it is likely that the rise in blood pressure may be even greater due to superimposed fear. This is also suggested by the results which have been recorded when suxamethonium was used for casting unanaesthetised horses. Cardiac arrhythmias, myocardial haemorrhages and sudden death have been reported in these

* Although the first analysis of depolarisation block was made with decamethonium this has not been used in veterinary anaesthesia, and so for the purposes of this discussion reference is only made to suxamethonium for which precisely analagous findings have since been made.

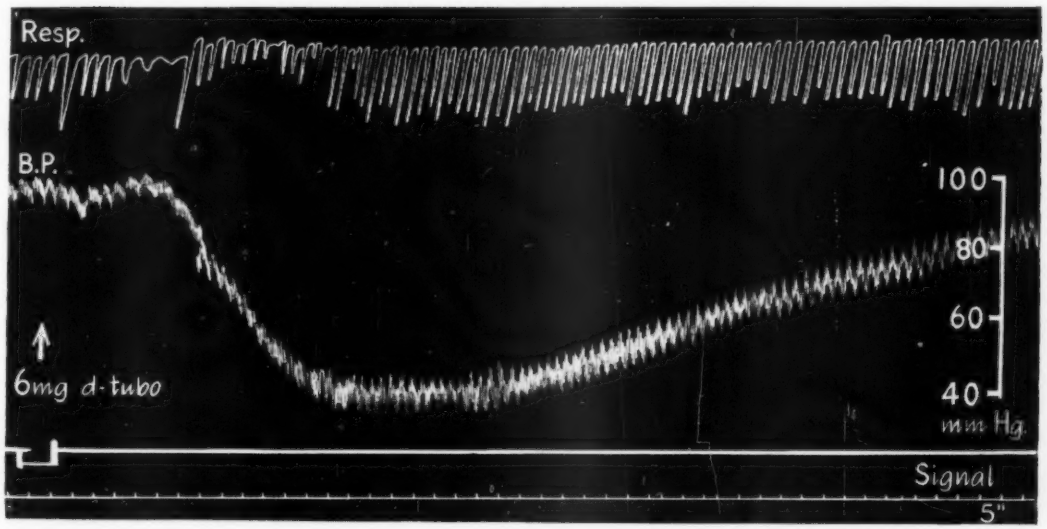

FIG. 3.—*Effect of an intravenous injection of* 6 *mg. d-tubocurarine in an* 18-*kg. dog under thiopentone/nitrous oxide/oxygen anaesthesia.* Upper tracing: Respiration—downstroke indicates inspiration. Middle tracing: Mean blood pressure recorded from the femoral artery. Lower tracing: Time intervals of 5 seconds.

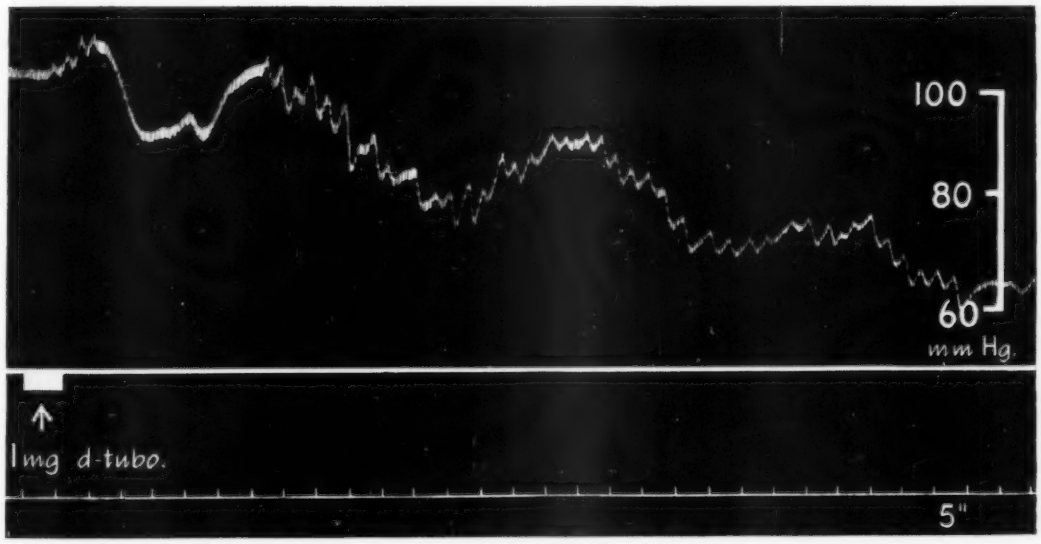

FIG. 4.—*Effect of an intravenous injection of* 1 *mg. of d-tubocurarine chloride in a* 2·7-*kg. cat anaesthetised with thiopentone/nitrous oxide/oxygen.* Upper tracing: Mean blood pressure recorded from the carotid artery. Lower tracing: Time intervals of 5 seconds.

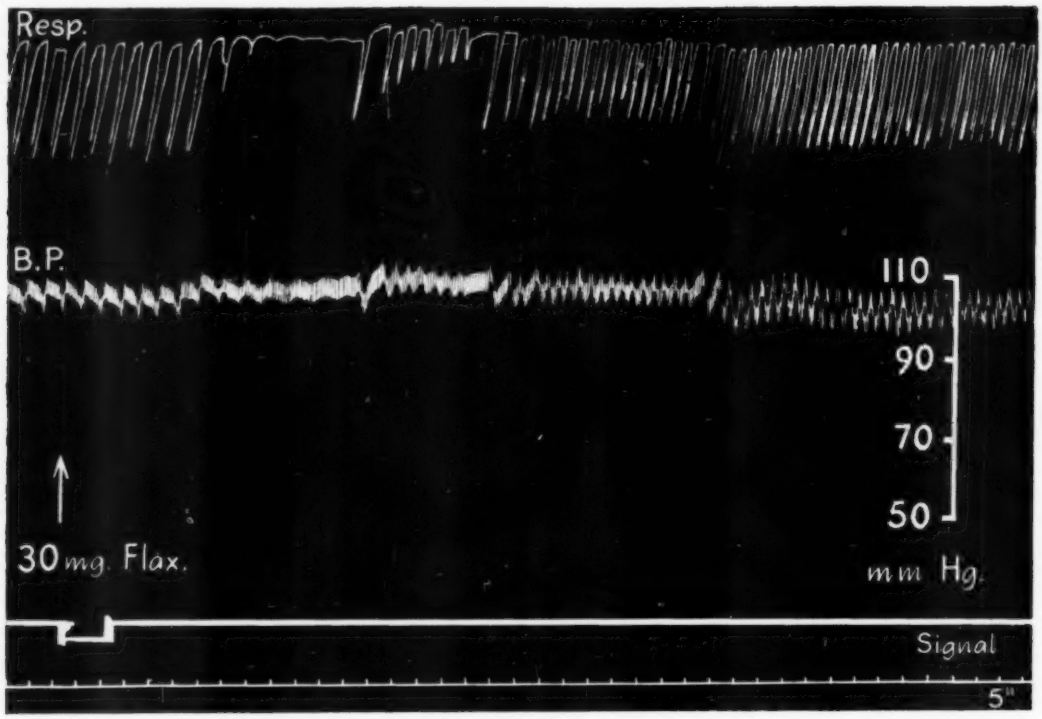

FIG. 5.—*Effect of an intravenous injection of* 30 *mg. gallimine triethiodide in a* 15-*kg. dog anaesthetised with thiopentone/nitrous oxide/oxygen.* Upper tracing: Respiration—downstroke indicates inspiration. Middle tracing: Mean blood pressure recorded from the femoral artery. Lower tracing: Time intervals of 5 seconds.

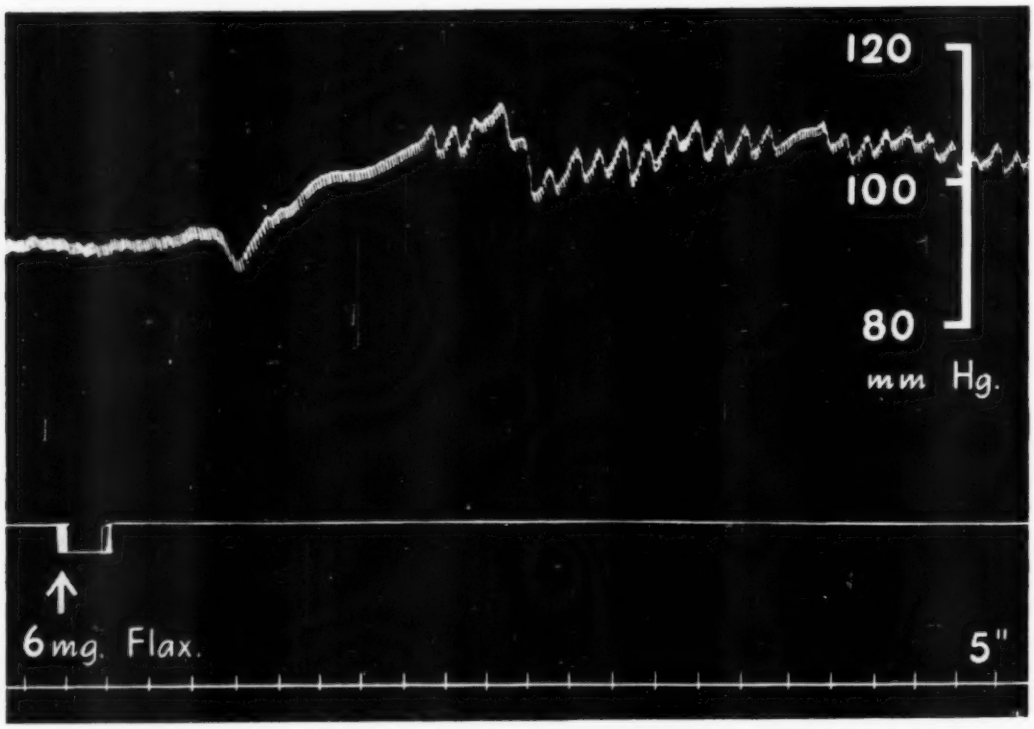

FIG. 6.—*Transient hypotension caused by gallamine triethiodide in a cat under thiopentone/nitrous oxide/oxygen anaesthesia.* Upper tracing: Mean blood pressure recorded from the carotid artery. Lower tracing: Time intervals of 5 seconds.

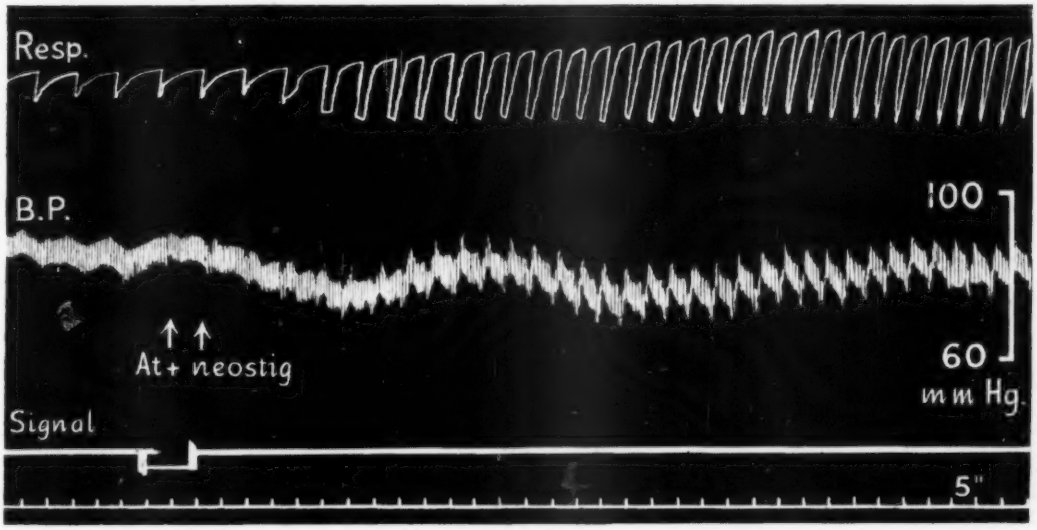

FIG. 7.—*Effect of neostigmine in a dog recovering from paralysis induced with gallamine triethiodide. Thiopentone/nitrous oxide/oxygen anaesthesia.* Upper tracing : Respiration—downstroke indicates inspiration. Middle tracing : Mean blood pressure recorded from the femoral artery. Lower tracing : Time intervals of 5 seconds.

unfortunate animals (Larsen *et al.*, 1959; Neal & Wright, 1959; Tavernor, 1959).

One injection of suxamethonium causes a rise in serum potassium. This rise in serum potassium may be associated with the cardiac arrhythmias, and since it is not abolished by adrenalectomy, ganglionic blockade, adrenolytic drugs or high epidural analgesia (Stevenson, 1959) it is likely that the rise is due to liberation of potassium from muscle. *Prolonged* administration of suxamethonium in dogs causes a large decrease in plasma potassium (Stevenson, 1959) but the reason for this is unknown.

As has already been mentioned suxamethonium causes a dual block in dogs. Stevenson (1959) considers that it is quite safe to administer anticholinesterase drugs to dogs following the prolonged administration of suxamethonium when, as not infrequently happens in these circumstances, difficulty is experienced in the re-establishment of adequate spontaneous respiration.

The Use of Relaxants in Clinical Anaesthesia

It must be recognised that in clinical practice a relaxant should never be administered unless facilities for immediate and sustained artificial respiration are available. Artificial respiration means the application of intermittent positive pressure to the airway, for an animal cannot be efficiently ventilated for any period of time by the application of pressure on the chest wall. Intermittent positive pressure ventilation must be carried out *via* an endotracheal tube—a close-fitting face-mask is not satisfactory for gases may be forced down the oesophagus into the stomach and intestines.

Next, it must be recognised that relaxant drugs have no narcotic or analgesic properties. It is impossible to over-emphasise the importance of ensuring beyond all reasonable doubt that an animal is anaesthetised and incapable of feeling pain or apprehension throughout the whole period of action of the relaxant drug which is being employed. Emotions have been aroused by the use of suxamethonium in conscious horses and cattle, but, perhaps fortunately for these animals, as has been mentioned it now appears that this practice is unwise on pharmacological grounds alone.

When a relaxant is given the normal signs of anaesthesia are abolished and the problem arises of how to assess the depth of unconsciousness of the animal. With practice this presents but little difficulty.

1. The anaesthetist should be well acquainted with the effects produced by the premedicant drugs, induction dose of thiopentone, etc., in the absence of relaxant drugs.

2. Any increase in the pressure needed to inflate the lungs may indicate that unconsciousness is becoming less profound, or, that relaxation is passing off—the likelihood of this can be judged from the time interval which has elapsed since the last dose of relaxant drug was given.

3. If unconsciousness becomes too shallow noxious stimuli will produce reflex movements of the face-muscles, trunk and limbs. These movements are seen even when full *clinical* doses of relaxant have been administered.

4. The "cardiac pain reflex" of Longley and Croft may indicate a return towards consciousness.

When respiration has been abolished by the administration of a relaxant drug intermittent positive pressure respiration must be carried out with care. The understanding and application of the correct type of lung inflation is an essential part of the technique when relaxant drugs are used. It must be noted, too, that any machine used to produce inflation of the lungs by mechanical means must be capable of giving the correct type of pressure curve.

In short, in veterinary practice there are two absolute contra-indications to the use of relaxants:—

1. Absence of facilities which will enable intermittent positive pressure respiration to be carried out.

2. Inexperience of, or absence of an anaesthetist during any operation.

Experience has shown that caution in the use of these drugs should be exercised in ruminant animals, in animals suffering from disturbances of electrolyte balance or from respiratory obstruction. Also it must be noted that their use increases the likelihood of the occurrence of passive regurgitation of gastric contents in ruminants and in cases of gastric or intestinal obstruction.

The indications for the use of relaxant drugs in veterinary anaesthesia include the following:—

1. In dogs, for intra-abdominal and intrathoracic surgery, endoscopies and possibly for the reduction of dislocations. Dislocations are more easily reduced if muscle tone is abolished but re-luxation is facilitated by the absence of muscle tone. The reduction of fractures does not appear to be facilitated by the use of relaxants.

2. In cats, as for dogs, and in addition, for the performance of atraumatic endotracheal intubation.

3. In pigs, as for cats. Endotracheal intubation is very difficult in pigs without the use of relaxant drugs.

4. In horses, to produce muscle relaxation when this is required and to ease induction of inhalation anaesthesia in narcotised animals.

The details of techniques for the use of relaxants can only be effectively demonstrated in the operating theatre but there are, however, special points that need consideration.

Anaesthesia is best maintained by the use of the triad principle:—

Using judicious combinations of (1) a narcotic such as thiopentone in a dosage only just sufficient to induce unconsciousness, (2) analgesics such as nitrous oxide and oxygen, fortified, if absolutely necessary with more potent agents such as pethidine, ether, cyclopropane or halothane and, (3) the relaxant agents in sufficient dosage to provide perfect surgical conditions and complete control of the respiration. The indications for supplementary doses of these 3 components of the anaesthetic technique will vary slightly from one anaesthetist to another but in general:—

More relaxant is given if relaxation becomes inadequate or respiratory efforts become apparent.

More analgesic is given if signs of vaso-vagal syncope appear or if the pulse rate rises and this rise cannot be attributed to haemorrhage or any other

obvious cause such as the tachycardia caused by gallamine.

More narcotic is given if reflex movements or contractions of facial or limb muscles occur either spontaneously or in response to painful stimuli. It must again be emphasised, however, that response to stimuli does not necessarily imply "conscious awareness" of the stimuli.

With such a system, provided due care is exercised, the danger of an animal awakening during an operation is remote.

In clinical practice the use of relaxant drugs has proved to be safe and many animals which in the days of "depression" techniques would undoubtedly have died during anaesthesia have been brought safely through anaesthesia, and operation by the use of these drugs.

At Cambridge over a 6-year period in clinical practice alone 572 dogs, 205 cats, 68 pigs and 54 horses have received relaxant drugs and of this total of 899 animals (Fig. 8) only 7, 1 horse, 4 dogs, 1 cat and 1 pig have died due to the use of these drugs. The horse, pig and cat and one of the dogs died because of poor technique and these deaths cannot be truly ascribed to the action of the relaxant drug itself.

	Dogs	Cats	Pigs	Horses	
Total no. of anaesthetics :	2,331	735	432	92	= 3,590
Anaesthetics e relaxants :	572	205	68	54	= 899
d-tubocurarine chloride :	45	—	12	—	
d. m. e. curare :	12	—	5	—	
gallamine :	126	5	18	5	
laudexium :	3	—	—	—	
suxethonium :	1	—	—	—	
suxamethonium :	385	200	31	49	

FIG. 8.—Number of animals (excluding all experimental animals and ruminants) which have received relaxant drugs as part of the anaesthetic technique during a six-year period (October 1st, 1953, to October 1st, 1959) at the Cambridge Veterinary Hospital.

To summarise, the following advantages accrue from the use of relaxants in veterinary anaesthesia:—

(1) Deep "depression" anaesthesia is rendered unnecessary.

(2) Immediate control of the degree of relaxation is ensured.

(3) Immediate control of respiration is possible.

(4) The establishment and maintenance of light anaesthesia without fear of respiratory spasm, cough and hiccup is facilitated.

(5) Ideal conditions are afforded, with safety, for intrathoracic surgery, intra-abdominal surgery and endoscopies, and owing to the profound relaxation which can be induced atraumatic endotracheal intubation is possible in pigs and cats.

(6) In horses smooth induction of inhalational anaesthesia is possible in lightly narcotised animals.

It is more than probable that as these advantages become more widely appreciated, and an increasing number of students and others become more familiar with them these very useful drugs will come to be much more extensively employed in veterinary anaesthesia than they are at the moment.

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HISTORY OF THE ROYAL ARMY VETERINARY CORPS

It has been decided to produce a second volume of the history of the Corps covering the years from 1919 to the present day, and it is expected to take about 2 years to complete the text and publish it.

It is estimated that the total cost of producing, illustrating and printing the history will be £2,000. The responsibiliy for finance will be solely that of the R.A.V.C., but the B.V.A. has agreed to bring the need for donations to the notice of our readers, and to publish a subscription list. The Wellcome Trust has agreed to contribute £500 towards the total cost subject to sufficient money being raised from other sources, and among donations so far received are those from Pfizer Ltd. (£52 10s.), May & Baker Ltd. (£50), Cooper McDougal & Robertson Ltd. (£25) and Burroughs Wellcome & Co. (£50). Cheques from readers of THE VETERINARY RECORD should be made out to "R.A.V.C. History Fund" and sent to The Director, Army Veterinary and Remount Services, War Office, Droitwich, Worcs.

The Therapeutic Use of Cysteamine in Bovine Ketosis

BY

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Department of Physiology, University of Bristol

SUMMARY.—1. *Thirty-three cows suffering from primary ketosis were treated with an aqueous solution of cysteamine hydrochloride. Two or three 750-mg. doses of cysteamine were injected intravenously, generally at 3-day intervals.*

2. *Of 21 animals, the milk yield and appetite were recorded during the treatment. Furthermore, blood samples were taken before and during the treatment from these animals and were analysed as to the serum levels of ketone bodies, glucose, pyruvate, α-oxoglutarate and citrate. All the initial samples showed a considerable deviation from normality.*

3. *All 33 cases of primary ketosis recovered completely after 2 or 3 injections with cysteamine. Concomitant with the disappearance of clinical symptoms was a restoration towards normality of the excessively high levels of ketone bodies, pyruvate and α-oxoglutarate and of the initially depressed values of glucose and citrate as ascertained from the analysis of the serum samples of 21 animals.*

4. *The possible mode of action of cysteamine as a therapeutic agent in the treatment of bovine ketosis is discussed.*

Introduction

VARIOUS therapeutic methods have been in use in the past for the treatment of primary ketosis, most of which were based on the administration of glucose or glucose-producing reagents such as propionate and glycerol. In previous work (Bach & Hibbitt, 1959) it was found that in addition to ketonaemia and hypoglycaemia there existed in bovine ketosis a striking imbalance in the serum levels of members of the citric acid cycle, such as pyruvate, α-oxoglutarate and citrate. The grossly elevated levels of pyruvate and α-oxoglutarate were believed to be due partly to a deficiency in coenzyme A since this is needed for the oxidation of these components in the cycle. The metabolic imbalance can obviously be considered to be a reflection of the disease, and it was thought that by restoring the balance an improvement of the ketotic condition could be expected. This hypothesis was put to the test in this work by the therapeutic use of a substitute (or a biological precursor) of coenzyme A, *viz.* cysteamine. When cysteamine was administered to ketotic animals, a rapid clinical recovery was observed in all of the 33 cases of primary ketosis treated. The clinical recovery was accompanied by a marked improvement of the biochemical picture. An abbreviated version of these therapeutic results as well as the theoretical aspect of the work is being published elsewhere (Bach & Hibbitt, 1960a) while full details of the methods and the therapeutic experiments are contained in the present work.

Methods

Animals

Cases of primary ketosis occurring in cows on Jersey Island, in the North of England, and in the district of Langford (the University of Bristol Veterinary Field Station), were brought to our notice through the co-operation of practising veterinary surgeons and the Department of Veterinary Surgery of this University. The animals were treated with cysteamine and information was obtained on the clinical response to the treatment; in addition, blood samples were received before and during treatment for biochemical investigations. The cows on Jersey Island were naturally all of the Jersey breed; the other dairy breeds were represented in the cows treated in England.

Dispensation of cysteamine

Cysteamine hydrochloride was obtained from Messrs. Light & Co. Ltd., and was dried for 24 hours before use in a vacuum desiccator. After drying, 750 mg. doses were placed into rubber-capped bottles, which were sealed and stored in a refrigerator. Before use, the content of the bottle was dissolved in 10 ml. of sterile glass-distilled water and the resulting solution was diluted to 250 ml. with more sterile water. The above procedure was carried out immediately before administration, since the stability of the dilute solution was found to be limited.

Treatment

Before commencement of the treatment the history of each case was obtained and the animals were submitted to a thorough clinical examination. After this, the animals which were found to be suffering from a *bona fide* post-parturient primary ketosis were treated at "O day" (Figs. 1 and 2) with a dose of 750 mg. of cysteamine hydrochloride, which was administered intravenously at 3-day and in some cases at 2-day intervals. The intravenous route of injection was considered to be essential since subcutaneous treatment was found to cause local irritation. Three days were found to be the optimum interval for treatment. Reasons for this are discussed below. No ill effect of the treatment could be detected in any of the normal animals used at test cases.

Collection of blood samples

Blood samples were collected before treatment and during the therapeutic course from the jugular vein into 1-oz. screw-capped bottles containing 20 mg. of sodium fluoride. This quantity, while sufficient to inhibit the breakdown of glucose and while stabilising some of the other blood constituents, did not prevent the clotting of the blood, therefore serum was used for all biochemical analyses. In view of

the lability of some of the serum constitutents even in the presence of sodium fluoride, care was taken to estimate the levels of the labile constituents within the period of time after collection in which they had previously been found to be stable (Bach & Hibbitt, 1958).

Analysis of blood samples

The methods used for the estimation of glucose, pyruvate, α-oxoglutarate and citrate were identical to those described in previous work (Bach & Hibbitt, 1958). For the estimation of total ketone bodies, the method of Johnson, Sargent and Passmore (1958) was used. After conversion of the ketone bodies to acetone, the acetone content of the mixture was estimated by the method of Thin & Robertson (1952).

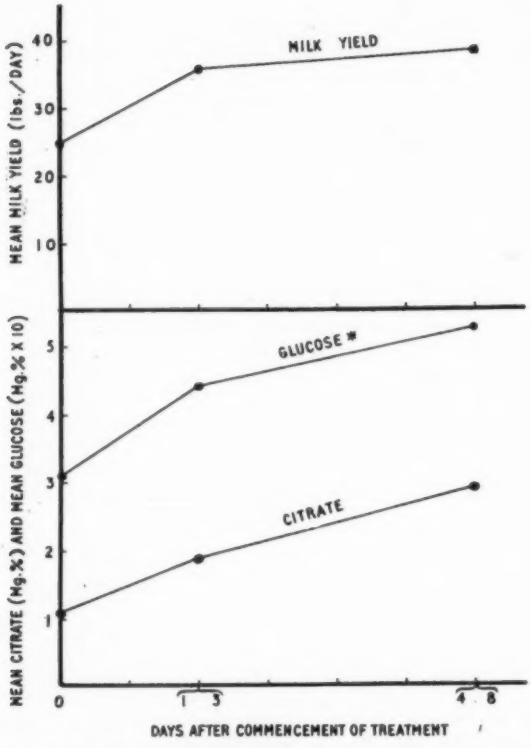

FIG. 1.—Changes in the mean serum levels of glucose and citrate and in the mean milk yields of 21 ketotic cows during treatment with cysteamine.

Significance of differences between "O days" and "4 to 8 days" (p values): glucose 0·01; citrate 0·001.

* Jersey cows only.

Statistical Methods

The significance of the changes observed in the levels of the serum components during treatment was ascertained by the "t test" (Fisher, 1938).

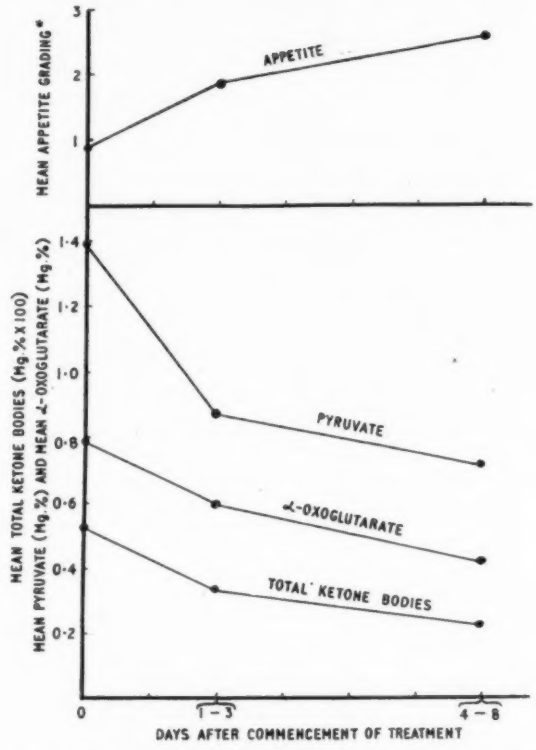

FIG. 2.—Changes in the mean serum levels of pyruvate α-oxoglutarate and total ketone bodies and in the mean appetite grades of 21 ketotic cows during treatment with cysteamine.

Significance of difference between "O days" and "4 to 8 days" (p values): pyruvate 0·05; α-oxoglutarate 0·001; total ketone bodies 0·001.

* Grading of appetite: 0 = Completely off food; 1 = Off concentrates; 2 = Slightly off food; 3 = Normal appetite.

Experimental

Thirty-five cows suffering from acetonaemia were treated with cysteamine. Two of the animals were however, later found to be cases of metritis and displaced abomasum respectively, both of which developed a secondary ketosis. Since this work concerns only cases of primary ketosis which is generally concluded to be associated exclusively with metabolic disturbances, the results of the above 2 cases were not recorded in this work. However it is noteworthy that the animals suffering from secondary ketosis also responded to treatment with cysteamine after the primary pathological condition had been treated; it is of course possible that the ketosis in these animals would have subsided spontaneously after the correction of the primary disorder. All the remaining 33 animals recovered completely after 2 or 3 injections with cysteamine. The biochemical data presented below refer to 21 of these cases, all of which, 8 from the North and South of England and 13 from Jersey Island, showed the typical symptoms of primary bovine ketosis. They initially manifested

various degrees of inappetence, particularly with regard to the concentrate foods; in every case the milk yield was depressed and in some cases nervous symptoms were also observed. A strong smell of acetone was detected in the breath, and milk samples revealed the presence of considerable quantities of ketone bodies.

Blood samples were taken before and during treatment with cysteamine.

Initial serum levels

The initial values for ketone bodies, citrate, pyruvate and α-oxoglutarate were all in the pathological range (Table I).

appetite and in the milk yield. As can be seen from Figs. 1 and 2 both appetite and milk yield increased during the treatment concomitant with the improvement of the biochemical picture of the serum.

Discussion

The beneficial effect of the cysteamine treatment of cows suffering from primary ketosis was clearly demonstrated by the clinical improvement of the animals and their full recovery in all cases as a result of the treatment. It was particularly encouraging to observe consistently that the serum levels of pyruvate, α-oxoglutarate and citrate approached, and nearly reached normality after 2 or 3 injections.

TABLE I
INITIAL SERUM LEVELS IN KETOTIC ANIMALS BEFORE CYSTEAMINE TREATMENT

Ketone bodies	40—80 mg. per cent.	(Normal level <10 mg. per cent. *
Citrate	0·5—1·5 mg. per cent.	(„ „ approx. 4·4 mg. per cent. †)
Pyruvate	0·8—2·5 mg. per cent.	(„ „ „ 0·55 mg. per cent. †)
α-oxoglutarate	0·4—1·25 mg. per cent.	(„ „ „ 0·19 mg. per cent. †)

* Thin and Robertson (1953). † Bach and Hibbitt (1959).

The initial serum levels observed were in close agreement with those reported previously (Bach & Hibbitt, 1959). The initial glucose levels were found to be far below normal in the Jersey cows, but hypoglycaemia was less marked in the cases treated in the North and South of England. The pre-treatment-glucose levels of the Jersey cows were 21 to 40 mg. per cent., those of the cows in England were almost in the normal range, 40 to 60 mg. per cent. The effect of cysteamine on the glucose levels could, therefore, be demonstrated only with the Jersey cows.

Changes in the serum levels during treatment

The data recorded in Figs. 1 and 2 represent the means of all the levels of serum components estimated at various intervals in the blood of the 21 animals from which biochemical data were obtained. These values were subjected to statistical analysis. The changes in the levels of pyruvate, α-oxoglutarate, glucose, citrate, and ketone bodies between "O days" (before treatment) and "4 to 8 days" (after commencement of treatment) were without exception highly significant, so were most of the changes between "O days" and "1 to 3 days" (see "p" values on Figs. 1 and 2.)

The striking biochemical response to the treatment is seen by the rapid increase in the serum levels of glucose and citrate (Fig. 1) and in the decrease of those of the ketone bodies, pyruvate and α-oxoglutarate (Fig. 2). Although in most cases the final serum levels do not show a complete return to normality during the 4 to 8 day period of treatment, they would most certainly have done so at a later period without further treatment, since, after receiving 2 to 3 doses of cysteamine, the animals appeared fully recovered and received no further veterinary attention. Only 2 relapses were reported, the possible cause of which is discussed below.

The principal clinical feature of the recovery of the animals was the marked improvement in the

Cysteamine was chosen because of its reported ability to act as a precursor or as a substitute for coenzyme A. The excessive use of coenzyme A in the synthesis of butterfat at the peak of lactation, and the losses of coenzyme A occurring in the milk (Bach & Hibbitt, 1960b), renders plausible the hypothesis of a coenzyme A deficiency in ketotic animals. In support of the idea of this deficiency are the excessively high levels of pyruvate and α-oxoglutarate, the utilisation of which requires the presence of coenzyme A. Furthermore, the accumulation of the above two serum components suggests a slowing of the oxidative reactions in the citric acid cycle for which the pathologically low citrate level may be another indication. Similar views regarding this relationship between the rates of reactions in the citric acid cycle and the citrate level in the blood have been expressed by Reid and Hogan (1959) in their studies on pregnancy toxaemia of ewes. Whether or not this concept is at the root of the etiology of the disease, the fact remains that the administration of a coenzyme A substitute or precursor restores the serum levels of the above three components to normality.

By restoring the rate of the oxidative reactions in the citric acid cycle, a reduction in the level of ketone bodies could be expected (Bach & Hibbitt, 1960a) and this is thought to be associated with an increase in the serum level of glucose (for references to this association see Reid, 1960). The observed fall of the level of ketone bodies and the rise in that of glucose after treatment with cysteamine renders this concept plausible.

There is ample evidence that the incidence of ketosis is related to high butterfat levels. For instance, the incidence of ketosis is particularly high in the Channel Island breeds which are known for a high percentage of butterfat in their milk. A reduction in milk yield and in fat synthesis would, therefore, provide favourable conditions for a recovery. It

(*Concluded at the foot of page* 800)

Symposium on Diseases of Zoo Animals

We are indebted to Dr. E. C. Appleby of the Royal Veterinary College for the following account.

The 2nd International Symposium of Zoo Animal Pathologists was held in Warsaw from June 10th to 14th this year and was attended by about 100 scientists from various European countries including Denmark, Holland and Switzerland. Apart from our Polish hosts, the largest group of visitors was from Germany and I was the only one from Britain. Probably the majority of those attending were pathologists, but there were a number of zoo directors, physiologists and workers in other fields.

The meetings were held in a superb conference hall equipped for simultaneous translation and decorated with flags of the nations. The 4 conference languages were Polish, English, German and Russian, although the expected group of Russian workers did not attend and their papers were read by others.

The subject for the first day was disease associated with nutritional deficiencies and the Chair was taken by the renowned Professor Dobberstein of Berlin. The first paper was given by Dr. Wackernagel of Basle who described the efforts made at Basle Zoo, following the example of Philadelphia, to reorganise completely feeding methods for all species using prepared cakes of known constitution containing vitamin and mineral supplements as a basic diet. He stressed the value of vitamin supplementation for fish-eating animals and birds and claimed a general improvement in health, and especially in reproductive activity, for the whole animal collection since the new methods were adopted. The new diets had proved a particular success with difficult species such as rhinoceros, gorilla, okapi and hyena and had encouraged breeding in sea lions, flamingos, pelicans and penguins.

Speakers from Frankfurt, East Berlin and Hanover Zoos all agreed that the use of cakes or pellets for zoo animals had many advantages—saving time, preventing waste and mistakes in dosage rates and improving health. Snags included the difficulty of convincing employees who were accustomed to old methods.

Several papers concerned the effects of vitamin deficiencies in zoo animals. Dr. Janczew of Sophia described cases of avitaminoses A and B in numerous different species of birds, some of which proved fatal and some of which responded to treatment. He ascribed the trouble in part to a diet of horse flesh and stressed its low value as a source of vitamins A and B. He also described a cystic enlargement of the thyroids in wolves which he considered to be due to the same cause, a horse flesh diet, a conclusion which was supported by some experimental evidence. Avitaminosis A was also said by one speaker to be the cause of the suppurative head lesions common in captive flamingos.

Dr. Kraft of Munich spoke on the importance of vitamin E; a deficiency causing deaths in young camels, water buffalo, deer and other animals in the first few weeks of life. In those under 3 weeks of age the dystrophic lesions of heart and skeletal muscle were often inapparent. In Dr. Kraft's opinion the vitamin was not absorbed rapidly enough from injection sites and the preferred method of treatment was an emulsion given by mouth.

Dr. Steuer of Dresden, where an " Archive of Zoo Animal Nutrition " is being set up, referred to the differing levels of protein and minerals required by males and females of the same species. He also said a little about Koller's concept of " Mesotrophy " concerning the difference between diets suitable for maintaining life and those which permit full reproductive activity. Dr. Stoll of Berlin discussed the interrelation between amino-acid deficiency, avitaminosis, and bacterial infection and expressed the

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The Therapeutic Use of Cysteamine in Bovine Ketosis. —*Concluded.*

has been noticed that the few relapses observed in this work occurred particularly in cases where cysteamine treatment at short intervals led to a rapid recovery of the animal, accompanied by a sudden rise in the milk yield. It was felt therefore, that cysteamine treatment should be given at intervals of at least 3 days in order to allow the organism to keep pace with the increased strain imposed by a sudden rise in milk production. Moreover, the " biochemical recovery," *i.e.* the regain of the normal rate of the oxidative reactions, must also lead to an additional demand for food which is borne out by the increase in the appetite (Fig. 2) during the recovery period. To meet this demand, increased feeding of concentrates during the recovery periods appear to be essential.

Acknowledgments.—It is a pleasure to thank Mr. C. L. Gruchy and his partners, St. Helier, Jersey, for their effective co-operation in providing blood samples from Jersey cows and for giving valuable information concerning their clinical conditions. We are also most grateful to Mr. H. Pearson, Dept. of Veterinary Surgery of this University, for rendering similar services with regard to animals treated in the south-west of England.

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view that the salmonelloses are not nowadays to be considered as straightforward infections. In 20 cases of enteric infection in snakes, salmonellae were recovered from 6 and "Arizona" organisms from 14.

Dr. Taborski of Warsaw described an interesting piece of work in which a disease in Axolotis characterised by oedema and haemorrhage was prevented by feeding the larva on plankton instead of horse meat and worms. This disease has also been recorded in Xenopus and Salmonidae larvae.

Dr. Gill of Warsaw Zoo gave an account of his experiments to estimate the rate of food passage in the alimentary tract of herbivores including the elephant, elk, bison and deer. He used dyed grain, and his results have a bearing on the optimum time for the administration of drugs, etc.

Dr. Ippen described an outbreak of necrobacillosis in a group of 5 newly acquired Saiga antelope, the severity of which was almost certainly due to low resistance caused by malnutrition and stress.

In the evening we attended a performance of the opera "Boris Godunov" excellently presented by a Polish cast.

The Second Day's Papers

The subject for the second day was Diseases of Primates, and the proceedings were commenced by Dr. Godgluck of Berlin whose paper on Poliomyelitis in Monkeys was unfortunately not translated. Dr. Lindau of Cologne described 3 cases of disease in the chimpanzee ascribed to the poliomyelitis virus and suggested that vaccination of both apes and staff might be a valuable precautionary measure.

Dr. Korda of Warsaw Zoo reported the systematic study of 850 newly imported monkeys, including 379 autopsies. Faults in the methods of transport were responsible for much of the disease and death, losses rising from 4 per cent. for a 4-day journey to 10 per cent. for a 12-day one. In small cages housing mixed groups of monkeys, the smallest were sometimes afraid to descend for food and clung to the wire of the cage until so weak that they could only hang by their teeth, ultimately falling to the floor exhausted. In general, alimentary disturbances were the most important, but bacterial pathogens were very rare and antibiotics of little value. Neuropathic factors, he said, are obviously of great importance, the rise in death rate between 5 and 6 weeks after arrival agreeing with Selye's concept of the decompensation stage of the stress syndrome. He also suggested that the frequency of intussusception was probably the result of psychic stimuli.

Dr. Krystoph of Leipzig discussed the occurrence of Salmonella in zoo animals and described an outbreak involving 4 chimpanzees and possibly 1 member of staff. Chloramphenicol was found to be the antibiotic of choice and he suggested routine bacteriological examination of faeces before illness is diagnosed. Dr. Hiepe, also of Leipzig, discussed the diagnosis and treatment of tuberculosis in zoo primates and suggested that with modern methods elimination of the disease is a practicable possibility. For diagnosis X-ray examination is very valuable and Herschel's method has been developed whereby the keeper, dressed in protective clothing, has an X-ray plate strapped to his chest and clasps the monkey against himself. He mentioned the use of tranquillisers ("Propathane"? ½ to 2 mg. per kilo intramuscularly or "Kiliphone"? 1.25 to 4 mg. per kilo by mouth) for restraint, and for treatment used 5 mg. per kilo I.N.H. orally for 6 to 8 weeks followed by a 14-day break and then repeated. B.C.G. vaccine has been used with success at Leipzig.

Considerable discussion followed and 2 speakers suggested a higher level of I.N.H., one advising 15 mg. per kilo and the other 10 mg. per kilo plus streptomycin injections. In the discussion, the importance of amoebic dysentery was remarked upon and the need for an improved method of diagnosis. One speaker who had visited monkey exporters in India commented that conditions of hygiene and management in the holding centres there were not too bad but that food was of a cheap quality and heavy vitamin supplementation would be of value. Dr. Kurt of the Netherlands found the only satisfactory treatment for newly imported monkeys with diarrhoea to be a water restricted diet continued for a long period.

Russian Papers

Several very interesting papers by Russian workers were read in their absence. The first by Dr. Czerkowicz of the Suchumi Institute concerned coronary insufficiency in monkeys (Baboons?), 7 cases occurring in 12 monkeys stressed by various means. It was unfortunate that the author of this paper was not present as there were many questions one would like to have asked. Another paper by Jakowlewa of the same institute contained a great deal of information derived from about 1,000 autopsies on monkeys. The author commented upon the different disease pattern in newly arrived monkeys where dysentery and tuberculosis were frequently fatal and that in the established colony where carriers of both diseases existed for years without symptoms. A third paper concerned pseudo-tuberculosis in monkeys.

Dr. Pruskiϕ of Warsaw described 7 cases of dystocia in monkeys remarking on the dangers of placental retention and the importance of post-operative care in cases of caesarean section. My own contribution concerned 6 cases of non-specific pericarditis in Chimpanzees, an insidious condition still causing deaths in the Edinburgh collecton. It has certain similarities to the human disease but has not apparently been seen in other zoos nor recorded in the literature.

In summing up, Professor Dobberstein emphasised the importance of annual symposia of this type which form the only means of communication between scientists working in this field. The assembly unanimously agreed formally to request the Polish authorities to publish the entire proceedings of the meeting and Mgr. Wolinski replied that there was good hope of this being done.

The next symposium is to be held in Cologne in the spring of 1961 concerning the subjects of avian diseases and parasitic infestations of zoo animals.

(*Concluded at foot of page* 803)

The Annual General Meeting of the Victoria Veterinary Benevolent Fund

The Annual General Meeting of the Victoria Veterinary Benevolent Fund was held at 9, Red Lion Square, London, W.C.1, on Wednesday, May 25th, 1960, at 4.30 p.m.

The President, Mr. H. W. Dawes, was in the chair.

Also present were: Professor T. J. Bosworth, Mr. E. Clark, Major J. J. Dunlop, Professor C. Formston, Mrs. D. I. Glover, Dr. R. E. Glover, Messrs. G. N. Gould, J. M. Ingram, Miss J. O. Joshua, Professors H. G. Lamont, J. McCunn, Captain T. M. Mitchell, Professors P. E. Mullaney, L. P. Pugh, Messrs. J. N. Ritchie, H. Sumner, Captain W. Watt, Professor W. L. Weipers, Messrs. E. Wilkinson, H. M. Wilson and Major W. H. Wortley.

Notice

By agreement the notice convening the meeting was taken as read.

Minutes

The minutes of the previous Annual General Meeting having been published in THE VETERINARY RECORD were taken as read and approved.

Election of President

Mr. Dawes was unanimously re-elected.

Election of Four Vice-Presidents

The four Vice-Presidents, Captain T. M. Mitchell, Professor L. P. Pugh, Mr. Henry Sumner and Mr. J. N. Ritchie, were unanimously re-elected.

Election of Honorary Secretary

Major J. J. Dunlop was re-elected.

Election of Honorary Treasurer

Professor J. McCunn was re-elected as were the auditors Messrs. Wilkinson, Chater & Co.

Annual Report and Statement of Accounts

In the course of his remarks the President said:—

"I do feel that as your President I should make a comment, as we have done in the report half-way down page 7, on the wonderful work of the Ladies' Guild. That appears to me to be growing splendidly, and it is a source of great satisfaction to this Fund that the efforts of the ladies are so successful. We owe them an exceptionally great debt for the work they do.

"The present situation of the Wortley Axe Bequest has given rise to a considerable amount of thought and work. We have made a suggestion for the purchase of land at Winkton, near Bournemouth. I cannot say any more at present; we are awaiting the approval of the Charity Commissioners to the suggestion we have put forward, but we hope at any rate that within the coming year we shall have made considerable progress towards the building of the necessary bungalows, in accordance with the Wortley Axe Bequest. Some of you may have thought that this was going rather slowly, but when one considers the difficulty of working hand-in-hand with the Charity Commissioners it is certainly a matter which cannot be hurried, and on which your sub-committee and your Council must move very carefully in order that no false step is made so that the Wortley Axe Bequest and your Council should not be placed in a difficult position. I think we are progressing.

"On page 10 you have the report of the Ladies' Guild. You will see there that raising that extraordinary sum of £1,318 7s. 1d. was the result of the work of the Ladies' Guild, and it was resolved that £1,000 of that sum be allocated for current relief, and £300 to the Special Gift Account.

"On pages 12, 13, 14, 15 and 16 are the particulars of those cases that are receiving help from the Fund. In this respect I should like to say how very much indebted the Council is to certain ladies who sit on the Council for the work they have done in visiting beneficiaries under the Fund. You do not need me to tell you that this is work in which a woman's hand is particularly valuable. The approach they are able to make has been most helpful to those efforts, and we are trying as a Council to increase the amount of visiting work that can be done by certain ladies. I am sure you will agree with me that a personal visit from someone representing the Fund is the finest way in which we can ascertain how our beneficiaries are going on in their difficult lives, and those ladies who visit them can actually help in more ways than one by the fact of a little personal consideration. From the letters that I and other members of the Council receive, I am sure that these visits by our ladies are very much appreciated, and I should like from the chair to say how very much I and other members of the Council appreciate the work these ladies do. (*Applause.*)

"I should also like to convey to our Irish friends, the very great appreciation of the Council as a whole of the efforts they are making on behalf of the Fund. To those of us who have known the work of the Benevolent Fund for a number of years the increasing support and interest which is coming from our Irish colleagues is a matter of the very greatest enjoyment to ourselves. Those of you who are here to-day —Professor Lamont, Professor Mullaney and Mr. Flynn—I would like you to take on your return home the very good wishes of this Council, and the fact that we as a Council appreciate most wholeheartedly what you are doing for us." (*Applause.*)

The annual report and statement of accounts were then adopted.

Election of 10 Members of the Association to Serve on the Council

Mrs. Glover, Dr. Wooldridge, Mr. Gould, Professor Lovell, Captain Whicher, Mr. Barrett, Professor Weipers, Mr. Spicer, Professor Formston and Mr. Flynn were re-elected.

Current Literature

ABSTRACTS

The Experimental Reproduction of Enterotoxaemia in Piglets. FIELD, H. I., & GOODWIN, R. F. W. (1959). *J. Hyg., Camb.* **57.** 81.

A description is given of the successful reproduction of enterotoxaemia in piglets due to *Cl. welchii*, type C. The disease was first produced by feeding broth cultures and egg-yolk cultures of the organism to young piglets but could not be initiated by smearing washed organisms over the sow's teats. This inability to infect piglets with the organism alone was confirmed by feeding suspensions of washed organisms shortly after birth. Parallel experiments in which the feeding of bacteria-free toxin was compared with washed organisms, however, showed that the missing constituent was the toxin ; for bacteria-free toxin readily initiated the disease and brought about the production of far more toxin in the intestine than had been fed initially. Investigations were then made into the source of this abundant toxin recovered at death. *Cl. welchii*, type C, was nearly always recovered *post mortem* from piglets dying from enterotoxaemia after being fed toxin, but very rarely from the litter-mate controls. These controls yielded type A strains, as did a series of normal piglets, and it was concluded that in the young piglets the type A strains so grossly outnumbered the type C strains that the latter could not be readily demonstrated by the techniques used.

The clinical and pathological signs in the experimental disease are discussed and it is mentioned that while blood-stained scour is a common sign, the scour is often slight or only a more normal yellow colour. It is postulated that type C organisms are normally kept in check in the gut but when a small quantity of toxin is fed this produces an area of intestinal necrosis in which rapid bacterial multiplication occurs. What the initiating factor is in the natural disease could not be deduced but the disease is probably more common where the organism abounds, as many naturally-occurring cases arose in the authors' experimental herd once the organism had been introduced to the premises. R. F. W. G.

Infectious Gastro-enteritis of Pigs. 1. The Disease in the Field. GOODWIN, R. F. W., & JENNINGS, A. R. (1959). *J. Comp. Path.* **69.** 87.

This paper describes the clinical, pathological, and epidemiological findings, in a large outbreak of infectious gastro-enteritis in East Anglia during 1957–8. In 10 herds, 137 litters of suckling pigs were affected and 610 piglets died.

Severe diarrhoea was the main sign at all ages but adult and fattening pigs usually recovered in 4 to 7 days. Pyrexia and nervous signs were absent. Pregnant sows commonly contracted the disease at or shortly after farrowing, so that the sow and newborn litter became affected together. Partial agalactia was common. Fattening pigs failed to grow while scouring. In suckling pigs the diarrhoea commonly had a greenish tinge and there was occasional vomiting. The mortality was closely related to the age of first infection, being over 90 per cent. during the first week of life, 50 per cent. during the second, and 25 per cent. during the third. Deaths over 3 weeks of age were rare. In every herd there was no obvious source of infection and the disease appeared even when special isolation precautions had been in operation for some time. The spread of the disease within a herd could be extremely rapid : in one herd of 23 sows, 9 litters, and about 100 fattening pigs, all these animals became affected within 7 days of the first case. The disease could also persist by affecting

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Symposium on Diseases of Zoo Animals.—*Concluded.*

General Impressions

The formal meetings were followed by a 2-day excursion to the Bialowieza Forest near the Russian border which is a reserve of European Bison *B. bonasus*. This was rather unrewarding and something of an endurance test but gave time to learn more of one's companions.

We also visited Warsaw Zoo which is quite large and well-stocked and where there is much successful breeding of carnivores, the young of which are circus-trained in a large underground arena. The zoo has a small but adequate hospital equipped for clinical and *post-mortem* procedures, and a modern physiology laboratory.

I paid a rapid visit to the Warsaw Veterinary School, an old-fashioned building which survived the war and which is somewhat short of modern equipment though not of enthusiasm or achievement. My impressions were somewhat blurred by the speed of my passage through the various departments but I saw the museum devoted to the anatomy of the European Bison and the pathology specimens hidden during the war in secret tanks and now in the process of reclassification. I learnt that rabies is now rare in Poland but that dogs are still compulsorily vaccinated and was impressed by the air of efficiency and practicality of the diagnostic and clinical services. I confessed to a spasm of jealousy when I saw the constant flow of horses available for clinical and pathological teaching.

The journey from Warsaw to London by rail took approximately 34 hours in each direction and no difficulties were experienced apart from the necessity of obtaining visas for East Germany while on the train and the frequency of passport, customs and currency checks.

My general impressions were of a country suffering many shortages and undergoing great difficulties but with a warm and friendly welcome for foreigners. I am most grateful for the many kindnesses that were shown to me there and for an interesting and valuable experience, and I am indebted to my own college for making it possible for me to attend.

successive litters at birth and on one farm a series of 35 litters were so attacked over a period of 11 weeks.

The chief pathological changes were an unusual pink discoloration of the skin ; gastritis, ranging from pin-point petechiae to acute fibrinous inflammation and extensive ulceration ; enteritis, sometimes intensely haemorrhagic, with engorgement of the mesenteric vessels and lymph nodes ; and meningeal congestion. Histologically, the changes corresponded with those seen macroscopically but, in addition, there was often tubular necrosis in the kidney while 3 pigs showed slight perivascular cuffing in the brain. In one outbreak, widespread petechial haemorrhages suggested cases of swine fever but gel-diffusion precipitin tests were consistently negative.

The authors conclude by pointing out that the disease they describe is virtually identical with that known in America as transmissible gastro-enteritis.

R. F. W. G.

Parenteral Benzathine Penicillin V in Bovine Mastitis. HOLLISTER, HUEBNER *et al.* (1959). *Amer. J. vet. Res.* **20.** 287.

Limitations of the intramammary approach to bovine mastitis prompted a series of experiments on 49 cows to determine the degree and duration of penicillactia following intramuscular injection of 3 and 6 mega benzathine penicillin V in aqueous solution, and of 3 mega repeated 3 times intramuscularly at 24-hour intervals.

Very full tables are given. The writers consider that where penicillactia ensues it is the result of active participation of the mammary gland and not merely of a circulatory overspill.

Management of Bovine Genital Infections. 1. Intravaginal Therapy. VIGUE, FITZGERALD & CASTRUCCI. (1959). *J. Amer. vet. med. Ass.* **134.** 308.

Of a very wide range of organisms recovered from the vaginas of 66 dairy cows known to be free from brucellosis, leptospirosis, trichomoniasis, and (so far as could be ascertained) vibriosis, only *Pseudomonas aeruginosa* was found to be resistant to nitrofurazone. About half of an average total of 530 cows in 4 herds were treated over 3 years by the twice-weekly deep vaginal introduction of a 0·4 per cent. nitrofurazone insert (weight not specified) from a few weeks after calving until after conception by A.I.

The average number of services per conception in the treated animals was 1·88 as against 2·85 in the untreated group ; the calving index of the treated group was 385 as against 447. J. P.

Potassium and Haemoglobin Types in Sheep with Special Reference to the Transmission of Scrapie. DARCEL, C. LE Q., & AVERY, R. J. *Canad. J. comp. Med.* **24.** 17.

The possible importance of heredity on the incidence of scrapie stimulated a genetic study of potassium and haemoglobin blood types in relation to the incidence of the disease in Cheviot and Suffolk sheep. During the course of the experiments 9 cases developed, 5 originating from 17 Cheviots inoculated intracerebrally and the remaining 4 cases in the Suffolks. Infection occurred irrespective of the potassium or haemoglobin types. However, the number of cases was too small to reveal any possible effect on the susceptibility to the disease. A. E. P.

The Emergence of Resistant Strains of *Salmonella typhimurium* in the Tissues and Alimentary Tracts of Chickens Following the Feeding of an Antibiotic. GARSIDE, J. S., GORDON, R. F., & TUCKER, J. F. (1960). *Res. vet. Sci.* **1.** 184.

After 4 passages in chicks fed on a diet containing chlortetracycline, the resistance to a culture prepared initially from a single colony of *Salmonella typhimurium* increased by steps from 20 parts per million to 210 p.p.m. No increase in resistance was noted when the experiment was carried out in chicks fed on a diet containing no chlortetracycline.

When chicks were orally infected with resistant strains and fed on a chlortetracycline-free diet there was no evidence of decline in the resistance of the strains isolated up to the 17th day after infection. Resistance then declined gradually but at the end of 14 weeks some of the isolated strains were still 4 times as resistant to the antibiotic as normal strains. Resistant strains persisted for long periods in chicks fed on a diet containing chlortetracycline.

The design of the experiment which included the use of phage typing together with certain *in vitro* experiments indicated that the resistant strains of *Salm. typhimurium* that were produced during chlortetracycline feeding had arisen by the adaptation of the sensitive strain used in the experiment, not by mutation or selection.

The veterinary and public health significance of these findings are discussed in great detail.

Studies in Immunity to Experimental Staphylococcal Mastitis in the Goat and Cow. DERBYSHIRE, J. B. (1960). *J. comp. Path.* **70.** 222.

Higher and more persistent levels of staphylococcal antibody were found in the sera of goats vaccinated with *Staph. aureus* formalised cell-toxoid containing aluminium hydroxide gel as an adjuvant, than in the sera of goats vaccinated with formalised cell-toxoid, cells alone, toxoid alone, or with a formalised whole broth culture.

Goats vaccinated with the adjuvant cell-toxoid exhibited only a mild transient reaction when subjected to intramammary inoculation of living staphylococci ; control goats, on the other hand, developed gangrenous mastitis. A similar degree of protection was conferred on cows given this vaccine.

Tests in goats indicated that only vaccines containing toxoid produced immunity.

A Killed Vaccine Against Paratuberculosis (Johne's Disease) in Sheep. SIGURDSSON, BJORN. (1960). *Amer. J. vet. Med.* **21.** 54.

Since its introduction in 1933 Johne's disease has produced serious losses in sheep in Iceland. This paper describes a large-scale field experiment designed to obtain further information on the value of a dead vaccine in the control of the disease.

The vaccine was prepared from a mixture of two bovine strains of *Mycobacterium johnei*, one of

American and the other of British origin. It was killed by heating to 70° C. for 1 hour, dried *in vacuo*, and then suspended in sterile mineral oil containing 0·3 per cent. phenol. One subcutaneous injection only was given, the dose being 1 ml. and containing 5·0 mg. of dried bacteria.

Half the lambs born in 1950 and 1951 (3,273 in all) were vaccinated when 5 to 6 months old, the other half (3,184 in all) being kept as controls ; 141 farms participated in the investigation. The farmers collected specimens of the intestine of all sheep that died subsequently and placed them in formalin solution ; diagnosis of Johne's disease was made by examining this material.

Up to the end of 1956, 3,493 of the 6,457 sheep in the experiment had died. No specimens were received from 1,191 of them, the proportion of missing specimens being approximately equal in the vaccinated and unvaccinated groups. Examination of the specimens indicated that 722 unvaccinated sheep had died from Johne's disease compared with only 59 in the vaccinated group. H. W. S.

Determination of Blood Serum Values of Parenterally Injected DBED Penicillin V in the Horse, Pig, Dog and Fowl. (Translated title.) JAKSCH, W. (1959). *Wien. tierärztl. Mschr.* **46.** 388.

Experiments were carried out in 12 horses, 40 pigs, 15 dogs, and 9 fowls, using dibenzylethylenediamino-di-penicillin V (DBED) Penicillin V—Biochemie, Kundl/Tyrol) to determine the blood serum levels of this penicillin salt following parenteral administration. In a previous paper (Hollister *et al.* 1957. *Amer. J. Vet. Res.* **18.** 584), the blood level of penicillin V in 10 cattle was determined. The German workers state that the following dosages are necessary for an effective 3 days' persistence of the penicillin blood serum level : horse—15,000 u. per kg. bodyweight intramuscularly ; pig—40,000 u. per kg. bodyweight subcutaneously (or 20,000 u. per kg. for bacteria very sensitive to penicillin). The addition of procaine penicillin when injected in this species produced especially high blood concentrations, and is recommended : dog—40,000 u. per kg. bodyweight subcutaneously ; poultry—60,000 u. per kg. bodyweight intramuscularly. No generalised or localised ill-effects were noted in any experimental animals. All doses were considered therapeutically effective for 3 days, though for practical use an addition of procaine penicillin at a dose of 10,000 to 20,000 u. per kg. is recommended in every case.

Agalactia and Acetonaemia in Pigs. (Translated title.) URAY, H. (1959). *Wien. tierärztl. Mschr.* **46.** 200.

A practising veterinary surgeon describes his methods of treating primary and secondary agalactia in pigs and the symptoms he observes in cases of acetonaemia. Occurring probably more commonly than is diagnosed, especially in fat sows, acetonaemia is found both *pre-* and *post-partum*, and presents a somewhat similar picture to that of secondary agalactia. The temperature is of little significance ; the drowsiness, in some cases almost a coma, is marked. Urine examination reveals acetone and sometimes protein. The disease is found predominantly where potatoes and protein-rich feeding-stuffs (*e.g.* skimmed milk powder) are used. Therapy was sodium propionate in one third of the cattle dose (Kontazet-Jacoby, Hallein) given in food or with the stomach tube. ACTH appears ineffective ; oral chloral hydrate has not been used. Dihydrotachysterol (AT 10, Bayer & Merck), a vitamin D relative, has been successfully used but the mode of action is uncertain.

Enterectomy in Cattle. (Translated title.) DIRKSEN, G. (1959). *Dtsch. tierärztl. Wschr.* **66.** 197.

A detailed description is given, together with 14 photographs (including 11 in colour), of a successful method of resection of the small intestine in cattle. Some details are as follows : right flank site ; local anaesthesia supplemented by tranquilliser if necessary. *En-masse* ligature of mesenteric vessels using Kocher's probe, then resection. End-to-end anastamosis and suturing in 2 layers, *viz.* mucosa, muscular coat, and serosa, in a continuous perforating Kürschner suture, then serosa alone in a continuous Lembert suture. Traction threads were used to facilitate bowel apposition. Perlon was employed throughout. The mesenteric slit was closed with the thread used for the mesenteric vessels. Intestinal wound was dressed with suitable fat or a prednisolon cream. The omasum was massaged (to avoid possible atony) before closure of the abdominal wound. Of 14 experimental animals used (3 for double resections) all recovered. Of 12 cases of mechanical ileus 11 recovered equally free from complications. One animal was slaughtered 3 days after the operation due to omasal paralysis. In mechanical obstruction of the small intestine this operation affords a good chance of total recovery. A. D. W.

DISEASES OF ANIMALS ACT, 1950—GREAT BRITAIN
Summary of Returns of Confirmed Outbreaks of Scheduled (Notifiable) Diseases

Period		Anthrax	Atrophic Rhinitis	Foot-and-Mouth	Fowl Pest	Sheep Scab	Swine Fever
16th to 31st August, 1960		8	—	—	12	—	55
Corresponding period in	1959	8	—	—	11	—	47
	1958	2	1	1	51	—	33
	1957	4	—	1	15	—	36
1st January to 31st August, 1960		150	—	14	1,389	—	796
Corresponding period in	1959	148	—	9	477	—	779
	1958	106	4	114	477	—	898
	1957	252	6	39	551	—	652

News and Comment

A HISTORIC ANNOUNCEMENT

Although it has been expected for some time, it seems appropriate to emphasise the following announcement, just received from the Ministry of Agriculture, which marks the culmination of what history may regard as the profession's greatest single triumph.

October 1st will mark the end of a concentrated effort of ten years by farmers, veterinary surgeons in both the State Service and in private practice, and by the Government to reduce the incidence of bovine tuberculosis in this country to a degree where it is no longer a national problem.

EXPERIMENTS ON LIVING ANIMALS DURING 1959

The return of experiments performed under the Cruelty to Animals Act, 1876, during 1959, published recently,* shows that throughout the year, or for some part of it, 6,438 persons held licences to perform experiments on living animals. A total of 3,943,022 experiments were performed during 1959. There were, over the period covered by the report, 535 establishments on the register at which experiments might be performed. New registrations numbered 19 and removals from the register 21. In the course of the year, 1,550 visits, mostly without previous notice, were paid by the inspectors to registered laboratories, and the inspections showed that both stock and experimental animals were properly accommodated and well cared for, and that licensees in general were fully attentive to the requirements of the Act and to the conditions attached to their licences by the Secretary of State. The inspectors visited 38 other premises proposed for registration.

The following irregularities were brought to notice during the year: In certain experiments of considerable importance in cardiac surgery a licensee, directing a team of research workers, extended their scope under the mistaken impression that his and their certificates gave the necessary authority. Subsequent applications for further certificates were granted to authorise the extended procedures. A pathologist not licensed under the Act, while temporarily in charge of a hospital pathological laboratory, reported that he had inoculated 2 guinea-pigs in the course of diagnostic tests normally carried out in the laboratory. He was mistakenly under the impression that he was entitled to do so under the licence held by the pathologist he was relieving. In each case it was considered that there had been no deliberate intention of infringing the Act and that a letter of admonishment and warning from the Secretary of State was sufficient.

* H.M. Stationery Office, price 6d.

THE BRITISH FARM PRODUCE COUNCIL

The British Farm Produce Council was officially launched on September 19th by the Minister of Agriculture, the Rt. Hon. Christopher Soames, at a press conference held at the Ministry.

The British Farm Produce Council was formed recently to promote the sale of the products of Britain's farms. It is sponsored by the National Farmers' Unions of Great Britain and Northern Ireland, all the Statutory Marketing Boards, the Fatstock Marketing Corporation, and the Pig Industry Development Authority.

UNIVERSITY NEWS

Edinburgh

The undernoted candidate has passed Part II Examination for the Diploma in Tropical Veterinary Medicine (D.T.V.M. Univ. Edin.): Chaudhuri, Rajat Kumar, B.V.SC., A.H. (BIHAR.).

Glasgow

Evening Post-graduate Refresher Course, 1960-1

The usual post-graduate evening course is being held this session at the Veterinary Hospital, Garscube, commencing on Thursday, October 13th, at 8 p.m., and thereafter on alternate Thursdays for approximately 7 meetings with a break during the Christmas and New Year period.

The theme this year will be Animal Nutrition and there will also be one lecture on Applied Genetics. The course will deal briefly with standard nutritional requirements for the various species but the main emphasis will be on errors in feeding and management which give rise to problems in animal health.

The subjects discussed will be:—

1. Nutrition of Cattle.
2. Nutrition of Sheep.
3. Nutrition of Pigs.
4. Nutrition of Poultry.
5. Nutrition of Small Animals.
6. Nutritional Problems associated with intensive Grassland Management.
7. Genetics in Relation to Veterinary Practice—the control of hereditary defects and the improvement of economic characters.

PERSONAL

Births

MAGNUS.—On September 15th, 1960, to Eileen and Alexander Magnus, M.R.C.V.S., of 46, High Street, Woodstock, Oxfordshire, a daughter.

ORFEUR.—On September 13th, 1960, at Willowcroft, Huish Episcopi, Langport, Somerset, to Bridget and Bernard Orfeur, a daughter (Caroline Bridget), sister for Peter.

WATT.—On September 2nd, 1960, to Loveina (*née* Stables) and John G. Watt, B.V.M.S., M.R.C.V.S., of 8, Buccleuch Place, Edinburgh, a daughter, Catriona Elisabeth.

Marriage

JAMES-ASHBURNER—RICE.—On Wednesday, September 21st, 1960, at St. Mary's Church, Byfleet, Surrey, Paul Wilson James-Ashburner, B.V.SC., M.R.C.V.S., of Newcastle, Staffordshire, to Josephine Brenda Rice of Byfleet, Surrey.

THE COOK REPORT

The report of the committee under the chairmanship of Dr. J. W. Cook, F.R.S., which was set up to consider the composition of milk, was published on Wednesday afternoon, too late for comment in this issue. A full review will appear next week.

COMING EVENTS

September

26th (Mon.). Meeting of the Yorkshire Division at the Talbot Hotel, Malton, 8 p.m.

28th (Wed.). Meeting of the B.S.A.V.A. North East Region at the Queen's Hotel, Leeds, 1, 8 p.m.

Meeting of the Southern Counties Veterinary Society at the Red Lion Hotel, Salisbury, 7.30 p.m.

Meeting of the South-East Midlands Veterinary Association at Franklins Gardens Hotel, Northampton, 7.30 p.m.

29th (Thurs.). Open Day at the School of Veterinary Medicine, Madingley Road, Cambridge, 2 to 5 p.m.

30th (Fri.). General Meeting of the North of England Veterinary Medical Association at Nether House, Alnwick, 2.30 p.m.

Meeting of the B.S.A.V.A. Midland Area at the Feather Hotel, Ludlow, 8 p.m.

October

5th (Wed.). Meeting of the R.A.V.C. Division at the Equine Research Station, Balaton Lodge, Newmarket, 11 a.m.

Autumn Meeting of the Scottish Metropolitan Division in the Royal (Dick) School of Veterinary Studies, Edinburgh, 2.45 p.m.

6th (Thurs.). Meeting of the Technical Development Committee of the B.V.A. at 7, Mansfield Street, Portland Place, London, W.1, 10.30 a.m.

General Meeting and Dinner of the Lancashire Veterinary Association at the Exchange Hotel, Liverpool, 6 p.m.

Meeting of the Central Veterinary Society at the Royal Veterinary College, Camden Town, N.W.1, 6 p.m.

7th (Fri.). Autumn Meeting of the North of Ireland Veterinary Association at the Midland Hotel, Belfast, 3 p.m.

15th (Sat.). Meeting of the B.S.A.V.A. North West Region at the Bull and Royal Hotel, Preston, 8 p.m.

18th (Tues.). Dinner-Dance of the Mid-West Veterinary Association at the Berkeley Café, Clifton, Bristol.

27th (Thurs.). Meeting of the Society for the Study of Animal Breeding at the Society's House, 1, Wimpole Street, London, W.1, 11.30 a.m.

28th (Fri.). Annual Dinner-Dance of the South Wales Division at the Park Hotel, Cardiff, 8 p.m.

December

2nd (Fri.). Annual Dinner Dance of the North of England Veterinary Medical Association in aid of the V.V.B.F. at the White Swan Hotel, Alnwick.

ADDRESSES OF DISEASE INFECTED PREMISES

The list given below indicates, first the county in which are situated the premises on which disease has been confirmed, followed by the postal address and date of outbreak.

Anthrax

Herefords. Upper Wintercott, Ivington, Leominster (Sept. 12).

Lanarks. West Hookhead Farm, Strathaven (Sept. 12).

Northants. Brook Farm, Lower Benefield, Peterborough (Sept. 15).

Renfrew. Whitemoss Farm, Bishopton (Sept. 16).

Wigtowns. Balgreggan, Stoneykirk, Stranraer (Sept. 13).

Foot-and-Mouth Disease

Devon. Pitt Farm, Branscombe, Seaton (Sept. 15).

Lincs. Bluebell Farm, Field House, Anderby, Skegness (Sept. 13); Priory Farm, Anderby, Skegness (Sept. 15).

Fowl Pest

Berks. Fairfield Farm, Priory Walk, Bracknell (Sept. 14); Bulwark, The Warren, Ralphs Ride, Bracknell (Sept. 17).

Dorset. Packers Hill, Holwell, Sherborne (Sept. 12); Windmill Hill, Holwell, Sherborne (Sept. 13); Homestead, Ringwood Road, Three Legged Cross, Wimborne; Long Meadow, Ringwood Road, Three Legged Cross, Wimborne; Brenton, Pleck, Holwell, Dorchester; Windmill Cottage, King's Stag, Sturminster (Sept. 16); Manor Farm, Lydlinch, Sturminster Newton (Sept. 17); Lower Piccadilly Farm, Holwell, Sherborne; Vale View, Holwell, Sherborne; Watkins Farm, Holwell, Sherborne (Sept. 18); Little Rodmore Farm, King's Stag, Sturminster Newton (Sept. 19).

Essex. Marshalls Farm, Handley Green, Margaretting (Sept. 18).

Salop. The Grove, Craven Arms (Sept. 19).

Warwicks. 114, Moilliett Street, Winson Green, Birmingham, 18; North Lodge, Haselor, Alcester; 116, Mary Street, Balsall Heath, Birmingham, 12 (Sept. 14).

Worcs. 111, Wild Moor Lane, Catshill, Bromsgrove; The Whitehouse Farm, Hanbury, Bromsgrove (Sept. 17).

Swine Fever

Denbighs. Machine House, Rossett, Wrexham (Sept. 19).

Devon. North Hay, Shebbear, Beaworthy (Sept. 12); Lewis Hill Piggeries, Northam, Bideford (Sept. 19).

Essex. Lower Barn Farm, Purleigh, Chelmsford (Sept. 16).

Glos. New House Farm, Highleadon (Sept. 15).

Isle of Wight. Kern Farm, Alverstone, Sandown (Sept. 13).

Lancs. Sowerby Lodge Allotments, Barrow-in-Furness (Sept. 12); Temple Farm, Bury Road, Edgworth, Bolton (Sept. 15); Cockersands Abbey Farm, Thurnham, Galgate (Sept. 19).

Lincs. Midville Farm, Hob Hole Bank, Boston (Sept. 12).

Montgomery. The Whittrey House, Chirbury (Sept. 12); Wig Fach, Dolanog, Welshpool (Sept. 13).

Norfolk. The Park, East Harling, Norwich (Sept. 12); Hillside Farm, Market Weston, Diss (Sept. 15).

Salop. Ketley Town Farm, Ketley, Oakengates (Sept. 12); Hillside Farm, Lilleshall, Newport; Lower Edgebold, Hanwood, Shrewsbury (Sept. 15); Moat Cottage, Stapleton, Dorrington, Shrewsbury (Sept. 16).

Staffs. Baswich Farm, Baswich Lane (Sept. 15).

Suffolk. Grange Farm Rendham, Saxmundham (Sept. 13); Willow Tree Farm, Occold, Eye (Sept. 15).

Sussex. Willow Farm, Lower Road, Herstmonceux, Hailsham (Sept. 14).

Yorks. Markenfield Hall, Ripon (Sept. 12); Yew Tree Cottage, Garforth, Leeds, Prospect House, Pickhill, Thirsk (Sept. 13); Kiplin Wood, Scorton, Richmond (Sept. 16).

Letters to the Editor

The views expressed in letters addressed to the Editor represent the personal opinions of the writer only and their publication does not imply endorsement by the B.V.A.

Practice in Canada

Sir,—Having been engaged, on successive occasions, in correspondence with U.K. members seeking information about practice opportunities in Canada, and particularly in Saskatchewan, may I have the courtesy of your columns to outline briefly the prospects for anyone interested?

The province of Saskatchewan has been organised into Veterinary Service Districts. These comprise 2 to 4 Rural Municipalities, and a Municipality is some 12 miles square. A District may contain, on average, around 15,000 head of cattle, 8,000 pigs, and numerous turkey and chicken farms. A contract is drawn up, whereby the veterinary surgeon is answerable to a board of councillors, representing the different areas, and they pay his subsidy from municipal funds, arrange vaccination schemes and so on. A scale of maximum fees is laid down, but otherwise the veterinary surgeon is free to run his practice. The subsidy amounts to approximately $2,000 to $3,000 per annum, and one half is paid by the Provincial government. Federal government testing is nearly always available at a rate of $30.00 per day, and calfhood brucellosis vaccination schemes are almost universal.

Every assistance is offered in purchasing a car and house, and little or no capital is required to get established. An average income of $8,000 can be expected, depending on the usual variables.

To my knowledge, there are upwards of 20 Veterinary Districts vacant at present, and the shortage of veterinary surgeons is acute. Most practitioners are located in towns of from 2,000 to 3,000 inhabitants with fully modern facilities, and there is, of course, no restriction on small-animal practice. One might add that, due to the sparsity of laboratory services and specialist advice, the individual has considerably greater scope than in the average British practice.

Detailed information may readily be obtained from the Provincial Veterinarian, Administration Building, Regina, Sask., who is able to supply a list of those areas still in need of veterinary services.

Yours faithfully,

D. W. GEORGE MACASKILL.

Crescent Avenue,
Souris,
Manitoba,
Canada.

September 9th, 1960.

Canine Intraocular Surgery

Sir,—I read with great interest Mr. Gordon C. Knight's excellent paper on Canine Intraocular Surgery in the August 6th edition of THE VETERINARY RECORD. Woe betide a mere student wtih three years' experience of dodging lectures to question Mr. Knight's vast knowledge and experience in canine ocular surgery, but there are one or two points I would like to raise.

Firstly, he mentioned that established hydrophthalmia cannot be corrected in the case of a dislocated lens by lens extraction, or by any other means, in his opinion. Would not a lens extraction in conjunction with a peripheral, or complete, iridectomy overcome this difficulty? Also in the cases where pre-operative hypertension greatly increases the risk of complications during the removal of the lens, would not this respond to eserine and Diamox? He also states that hypotension, along with a deep plane of anaesthesia, seems to reduce haemorrhage to a minimum. Surely it would follow that, when there is pre-operative hypertension, the sudden release of aqueous humour caused by the keratome puncture would greatly reduce the pressure on the blood vessels, which are constricted, with their consequent engorgement and so causing more haemorrhage on their being severed, and accentuated by the rapid fall in intraocular pressure when the eye is opened. In view of this it would appear desirable to ensure that the pressure is reduced as much as possible before any intraocular operation.

Secondly, I would like to ask if the occasional failure of this operation due to post-operative hydrophthalmia may have been caused by suturing through the cornea as, I believe, that this is also experienced in human ocular surgery, and is now being overcome by taking only a partial thickness of the cornea in the sutures so that there is no interference with drainage of the anterior chamber.

Thirdly, I would be interested to learn if any difficulty has been experienced in this conjunctival flap method in respect of the buried corneal sutures breaking through the conjunctiva and so causing irritation and also at times a weakening of the wound. Mr. Knight says that the last 120 operations have been done by this method, but he does not mention what method he used before. Was this the corneal section method using a Von Graefe knife or Sinclair's scissors?

Yours faithfully,

J. B. LLOYD.

University of Glasgow Veterinary School,
Buccleugh Street,
Glasgow.

August 22nd, 1960.